Volume XX SECTION ONE Number 8

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DISEASES OF THE NERVOUS SYSTEM

A Practical Journal on Psychiatry and Neurology

AUGUST
1959

(CONTENTS ON PAGE 328)

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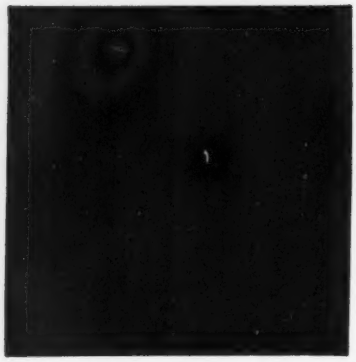

restorative activity apparent in hours

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objective antidepressant response in days

•

complete recovery in 2 to 6 weeks

•

side effects transient and mild

Common among the experience reported by several investigators during the Nardil trials was this new drug's speed of action, high percentage of complete to good remissions, the absolute lack of toxicity and the infrequency and mildness of side effects.

Many patients report a lift in mood within four to eight hours. A new sense of purpose is accompanied by a rapid dispersal of self-deprecatory feelings, ruminative thinking and suicidal ideation. Sleep and appetite are improved.[1]

Sainz[2] reported that, of his series of 122 patients, 89 per cent of the depressed affectives and 82 per cent of other endogenous depressions had complete remissions following Nardil.

Maximum improvement was always noticed not later than five weeks after the onset of therapy.[2] This investigator then concluded that Nardil "...appears to be the treatment which most clearly compares to electrocoma therapy in scope, rapidity of action and freedom from serious side effects."[2]

This observation has also been made by Thal[1] as a result of his experience with Nardil in 180 patients with true (endogenous) depressions. "In the treatment of depression, the response to this antidepressant therapy approaches the response generally obtained from electro-shock therapy. Eighty per cent of patients were discharged from the hospital as recovered within 60 to 90 days following commencement of treatment with Nardil." Electroconvulsive therapy was not used in any case.

Saunders and colleagues[3] found that all their patients with true (endogenous) depressions recovered within 10 to 15 days of therapy with Nardil.

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Nardil has a preferential distribution to the brain—not the liver. The investigations of Sainz[2] in 122

COMPARATIVE EFFECTIVENESS*

General diagnosis	Patients	ECT % Satisfactory Response	Iproniazid % Satisfactory Response	Patients	Nardil % Satisfactory Response
endogenous depression, overt	11	72	45	26	78
endogenous depression, larval	3	—	100	12	86
affective psychosis, depressed phase	8	87	42	19	89

*Adapted from Sainz, A.

moderate to markedly depressed patients revealed that Nardil was "...less toxic than iproniazid because no hepatic, hemopoietic or central nervous system parenchymatous damage (had) occurred or been foreshadowed." The experience of Thal[1] in 180 patients, and that of Saunders[3] as well, disclosed no toxic effect after careful analysis of liver function tests and blood studies.

Postural hypotension has appeared among a few patients given Nardil in a dosage range higher than that recommended.[2] But since the incidence does not appear to be clinically significant, it does not detract from Nardil's particular value in ambulatory as well as hospitalized patients.

Indications: Nardil is indicated in the treatment of true (endogenous) depressions of an affectual or organic nature. Depression associated with catatonic schizophrenia may be relieved, although Nardil itself has no effect on schizophrenic mechanisms.

Side Effects: The occasional side effects which have been reported include postural hypotension with the expected associated signs, transient impotence, nausea, ankle edema, delayed micturition and constipation. These can be adequately managed by appropriate adjunctive therapy or will abate as dosage is reduced to the maintenance level.

Caution: Even though no toxic effects on the liver have been reported with the use of Nardil, as a matter of caution patients should be carefully followed with liver profile studies and the drug should be withheld or used with extreme care where the patient has a history of liver disease or where liver damage is present. Also, hypotensive patients should be under close medical supervision.

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References: 1. Thal, N.: Cumulative Index of Antidepressant Medications. Dis. Nerv. System *20*:197 (May) 1959. 2. Sainz, A.: The Phrenopraxic Activity of a Non-noxious Antidepressant, Ann. New York Acad. Sc. (in press) 1959. 3. Saunders, J. C.; Roukema, R. W.; Kline, N. S., and Bailey, S. d'A.: Clinical Results with Phenelzine, Am. J. Psychiat. (in press) 1959. 4. Report of Clinical Trials with Nardil in 800 Patients. Warner-Chilcott Department of Clinical Investigation, 1959. 5. Chessin, M.; Dubnick, B.; Dramer, E. R., and Scott, C. C.: Modifications of Pharmacology of Reserpine and Serotonin by Iproniazid, Fed. Proc. *15*:409, 1956. 6. Chessin, M.; Dubnick, B.; Leeson, G., and Scott, C. C.: Biochemical and Pharmacological Studies of β-phenylethylhydrazine and Selected Related Compounds, Ann. New York Acad. Sc. (in press) 1959.

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Volume XX AUGUST 1959 Number 8

DISEASES *of the* Nervous System

Contents

DIAGNOSIS AND TREATMENT OF BEHAVIOR DISORDERS IN CHILDREN 334
George J. Lytton and Mauricio Knobel

INCIDENCE OF FOURTEEN AND SIX PER SECOND POSITIVE SPIKE DISCHARGES IN ROUTINE SLEEPING EEG'S 340
C. G. Glenn and Rhoda Knuth

AIDS IN DIAGNOSIS OF EPILEPSY IN SERVICEMEN 342
Chester M. Pierce and Harry H. Lipcon

THEORETICAL CONSIDERATIONS IN PARKINSONISM INDUCED BY TRANQUILIZING DRUGS 346
Paul Guggenheim and Leon Cohen

TREATMENT IN PRIVATE PRACTICE 353
Sullivan G. Bedell

PATIENT IMPROVEMENT AND PSYCHIATRIC NURSING CARE 357
Gordon R. Forrer and James L. Grisell

DEPROL IN DEPRESSIVE CONDITIONS 364
Karl Rickels and James H. Ewing

THE HISTORY AND PHARMACOLOGY OF THE ATARACTIC DRUGS 365
Maurice Klotz

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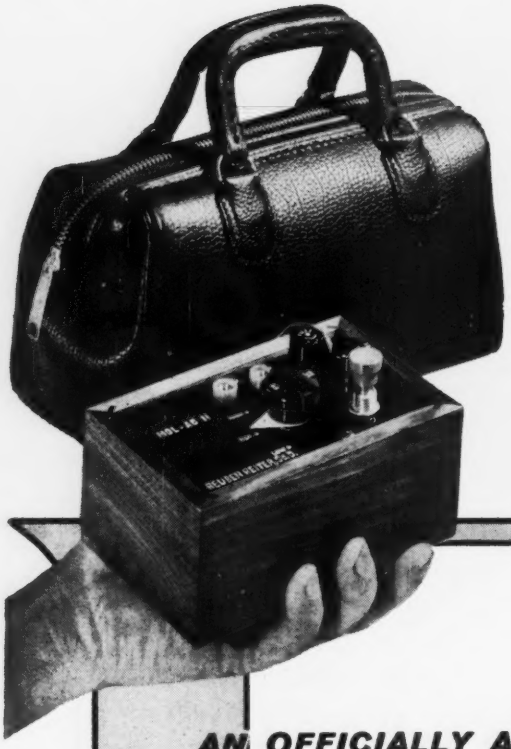

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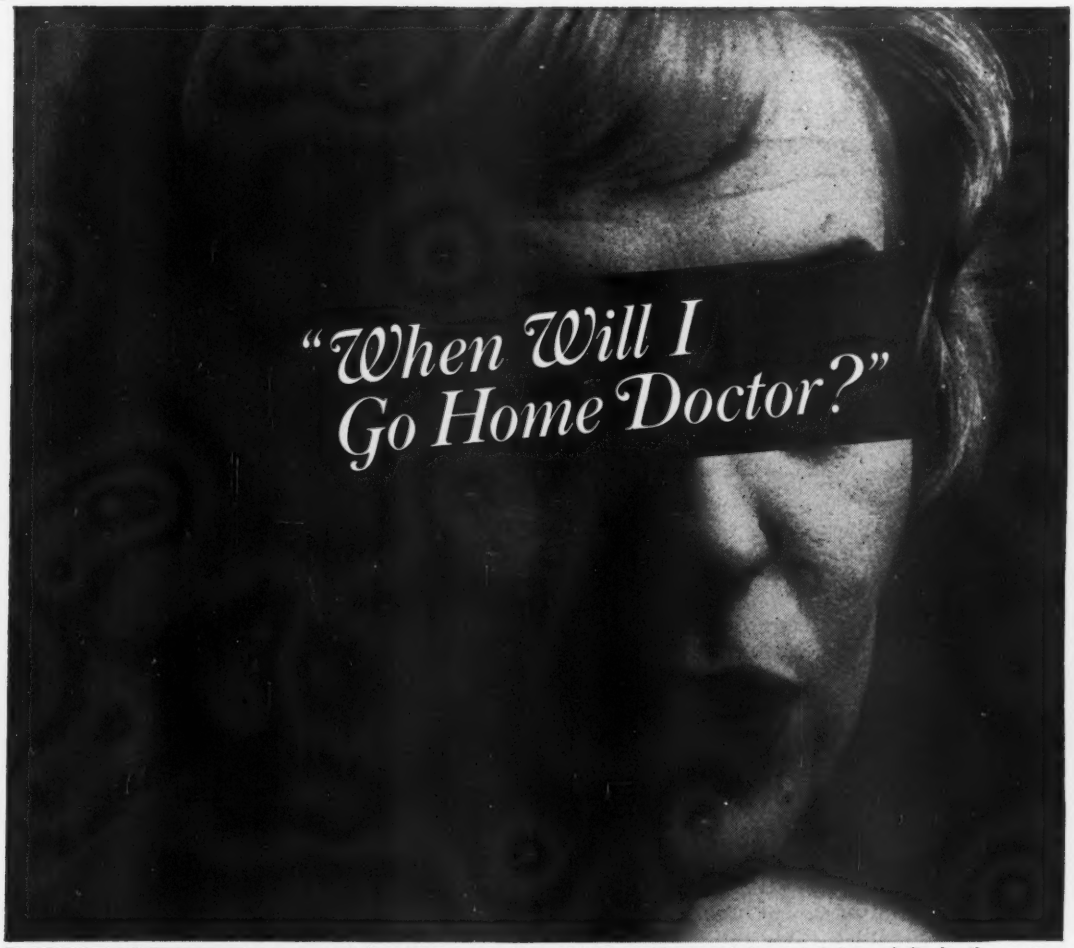

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1. Goldman, D.: Am. J. M. Sc. 235:67 (Jan.) 1958. 2 Morehouse, W. G., and Freed, J. E.: Monographs on Therapy 3:32 (May) 1958. 3. Leger, Y.: Union Med. Canada 87:831 (July) 1958.
4. Bruckman, N. S.; Saunders, J. C., and Kline, N. S.: Monographs on Therapy 3:24 (May) 1958.

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Rudy, L.H.; Rinaldi, F.; Costa, E.; Himwich, H.E.; Tuteur, W., and Glotzer, J.: Trifluoperazine in the Treatment of Psychotic Patients, Am. J. Psychiat. *115*:364 (Oct.) 1958.

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DISEASES of the Nervous System

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Diagnosis and Treatment of Behavior Disorders in Children

GEORGE J. LYTTON, M.D., and MAURICIO KNOBEL, M.D.

The concept of the hyperactive child has had much attention in recent years. The question of the role brain damage plays in this condition has always been pertinent and the relative importance of psychodynamics and organic involvement has been vigorously debated. The present wide acceptance and use of mood changing and behavior modifying drugs has presented some developments in the therapy of hyperactive children based on behavior modification by chemical means. This paper includes a discussion of this hyperkinetic syndrome and behavior disorders in general, and presents the results and theories drawn from a pilot study of the action of methylphenidate (Ritalin®) in this type of problem.

It is believed that a syndromic approach in child psychiatry would be helpful in clarifying diagnostic procedures, clinical judgments, therapeutic approaches, and especially a theoretical framework. A recent attempt was made to define in a more precise manner the hyperactive child,[1,2] considering the possibilities of an organic basis for this particular syndrome. There is currently a tendency to consider psychiatry as a biological science, even though an organic basis for behavior disturbances was long ago postulated.[3] Recent neuro-physiological investigations applied to psychosomatic medicine have demonstrated that cortical dysfunction associated with psychological problems may determine dysfunction in different parts of the organism, the visceral system in particular.[4,5,6] The limbic system, commonly associated with psychosomatic problems, can also be related to psychiatric symptoms.[7]

From the Department of Child Psychiatry, The Greater Kansas City Mental Health Foundation.

The effect of the frontal lobe as a control area related to behavior problems has been exhaustively studied, as well as the general influence of different cortical areas in specific and non-specific behavioral traits. There is a complex interaction of defective function, irritation, and inhibitory release.[8-12]

The temporal area has been found to be related to behavior problems, and even the so-called epileptic personality has been attributed to alterations in the anterior temporal area.[13,14] The gestaltic approach to behavioral problems is based upon the acceptance of some organic disturbances.[15-19]

The term organic does not of necessity mean anatomical or structural lesions; physiological encephalic dysfunction of unknown cause might be implicated, or dysfunctions due to changes in encephalic enzyme systems may be present.[20-22]

In the case of the hyperactive syndrome, it is difficult to accept a diencephalic dysfunction or lesion, produced in early life, unaccompanied by other significant pathology.[2] Diencephalic lesions would produce a more complicated symptomatology; therefore some consideration should be given to disorders of the cortical areas or cortical sub-cortical pathways. The slower development of the cortex, compared with the diencephalon, makes it more susceptible to damage in a quasi-embryonic stage of development. The prefrontal cortex in human beings apparently undergoes some structural development until approximately ten years of age; it is easy to speculate that mild trauma which would have no effect on the phylogenetically older structures of brain might impair the development and function of the cortex. It also seems to be true that diencephalic le-

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sions produce a more complicated and spectacular symptomatology than cortical lesions. This argument, of course, does not imply that a diencephalic dysfunction could not exist in behavior disorder; but if it did exist it could very well be due to the lack of cortical control, if a cortical lesion is present.[2] We have observed in acting-out children a behavior which seems so primitive, so uncontrolled, that it is remarkably easy to speculate that the deficiency in brain function lies in the lack of cortical control; therefore the behavior observed may be due to the primitive diencephalic impulses which are not subject to cortical control. We are tempted to call the victims of this disease process "the cortical children," paraphrasing the common physiological expressions "hypophyseal animal," "adrenal animal," which are applied to experimental animals in which these organs are suppressed.

The cortex is organized in such a complex fashion that it is difficult to correlate a specific cerebral area with a particular type of behavior,[23-25] but cortical organization is essential for adjusted behavior. When there is a cortical malfunction a primitive disorganized type of behavior is exhibited. This process was described by Goldstein[17] as "dedifferentiation" or as an attempt of more primitive anatomical structures to compensate for lack of cortical control.

Magoun,[26] working with the "activating system" demonstrated that the diencephalon, operating through the activating system, affects the cortex in a generalized manner without topographical localization and provides the individual with the experience of external reality through the convergence of sensory stimuli. According to Jasper and his associates[27] in the thalamus there exists a similar system which exerts its influence on more restricted cortical areas and stimulation of these specific cortical areas modifies the activity of the reticular system. This cortical sub-cortical interaction is extremely important in behavioral changes due to encephalic lesions. The thalamo-cortical correlation has an enormous importance in the expression of emotion. According to Spiegel and his co-workers[28] there exists a multiple representation of this function, fundamentally the connection of the dorsomedial nuclei with the prefrontal areas, the anterior nuclei with the cingulum, the hypothalamus with the frontal lobe and the intradiencephalic nuclei.

Cosideration of the above concepts would indicate a shift from purely psychogenic criteria to a more integrated psychoneurological point of view, in which an unspecified cerebral dysfunction could be postulated as the cause for the behavioral problem.[2] As the child grows his interpersonal relationships will have a lot to do with the way in which his basic disorganization will express itself. In cases of organic involvement, we may be able to talk about "schizophrenogenic" or "psychopathogenic" environments, but as Lauretta Bender[15] pointed out: "A dynamic interrelation may describe the psychological problem but still doesn't touch the cause."

The social, familial, and biological circumstances make it very difficult to describe a syndromic entity in the case of the brain damaged child. Cortical damage itself could vary in many ways from child to child, and each type of cortical damage could manifest itself in various symptom reactions and different "behavior problems."

Several attempts have been made to control behavior by medication; in particular the work done with amphetamine has been of interest. Although the emphasis in some of these studies was on the improvement of motoric efficiency in brain damaged children, a strong lift in mood was noted, with generally improved functioning in all body areas and behavior in general.[29-33] The use of amphetamine produced occasionally some undesirable side effects with clinically useful doses.

Some of the reports on methylphenidate made it appear that this drug had a strong central action without peripheral vascular effects and without sympathomimetic effects. A number of investigators have reported methylphenidate produces a marked psychomotor stimulant effect in both experimental animals and humans[34-38] Although the blood pressure, heart rate, and respiration was increased in at least one study on humans[38] most authors agree it has little hypertensive effect and at least one author postulates an

anti-hypertensive effect.[39] The mode of analeptic action is as yet unknown but probably it is of central origin.[34,39-42] Several investigators have reported clinical studies in which both brain damaged and psychodynamically disturbed patients have exhibited changes in mood, improved reality testing, increase in introspection, and increase in mood stability.[35-38]

The exact site of action of methylphenidate remains a subject of considerable discussion. The physiological effect is certainly located in the central nervous system, probably in the thalamus. However there seems to be strong evidence that at least some effect of methylpenidate may be on the cortex. Reference is made to the work of Cole and Glees[43] who mention that decorticated monkeys had no disturbance of sleep pattern when the thalamo-frontal connections were severed. It was their opinion that severing these connections removed from participation those cortical areas of the brain which stimulate and are stimulated by other centers; this stimulation acting to generate and store anxiety and tension. We should like to mention here that the reverse of this might be true. Since experimentally methylphenidate causes no disturbance in the sleep pattern, it would seem to be a question whether the drug itself has some stabilizing action on the cortex, so that the cortex does not have to react as adversely to thalamic stimulation as it would without medication. The fact that methylphenidate produces a reinforcement of conscious subjective functioning as reported by Hartert et al.,[38] Heiss et al.[36] and Carter[35,37] would suggest there is a strong cortical component involved in the action of this drug, and that it acts not only by stimulating the cortex through subcortical structures, but by mediating its activities directly on the cortex.

Method of Study

Methylphenidate was administered to 20 children whose primary complaint was a behavior disorder of some sort. The data collected on these cases is presented in tabular form (Table I). These children have been in treatment for periods of between sixty days and five months. The dosage varied from 15 to 200 mgs. daily, the oral route being used in all cases. The over-all results appear to be excellent; using a mixture of subjective and objective evidence it was felt that 15 showed definite improvement, three showed no improvement and in two cases the results were doubtful. Side effects consisted of urticarial rash (one case), anorexia, and insomnia. In only one case was it necessary to discontinue the drug.

Results were evaluated through periodic visits with the child, parents' reports and teachers' evaluations. For this last purpose we asked the teacher to fill out Burk's Behavioral Rating Scale,[33,44] a questionaire type of report that furnishes a numerical rating of behavior that increases when behavior becomes disorganized, and decreases when behavior is better organized (Table I). In 13 cases it was possible to obtain a second rating from the teacher. The mean decrease on this second rating was 27.1 points. Parents' observations were recorded that described the children's improvement. Sample phrases included: "Doesn't fight as much as before," "No more tantrums," "The teacher reports he is doing much better in school," "An entirely different boy," "Is more a part of the family," "Performs a task," "Does his homework," "For the first time in ten years I am relaxing," and "More talkative and friendly."

Age, presence or absence of neurological signs, signs of organicity on the Rorschach, and comparison of primary and mixed dominance showed no correlation with the improvement. In this series 15 out of 20 cases had initial EEG's reported as abnormal; 15 out of the 20 were repeated and in only one case was a change noted, this case being reported normal after five months of treatment; the initial EEG had been reported as abnormal. Four out of five of the children with negative EEG's improved and 11 out of 15 children with abnormal EEG's improved.

Using the Draw-a-Person test, the range of intellectual retardation was from no retardation to six years six months retardation. This series seems to indicate that a child, as he becomes older, is more likely to have difficulties in drawing-a-person, therefore we found some correlation between retardation as measured by the Draw-a-Person

TABLE I

Case	Sex	Age	I.Q. V.-P.-F.S.	Dominance Hand-Eye-Foot	Burk's Rating Scale	Speech Difficult.	Neurological Abnormalities	EEG Abnormal-	Signs of Organicity in Rorsch.
R.S.	M	10.7	101-103-102	RRL	107	+	—	—	6
R.J.	M	13.4	92-101- 96	RRR	76	—	+	—	3
D.W.	M	12.9	123-103-115	RLL	68	—	—	—	0
D.J.	M	8.4	90- 78- 83	RLL	108	—	+	+	6
D.D.	M	10.4	116-103-111	RLL	61	—	+	+	1
R.P.	M	8.3	86- 90- 87	RRL	112	+	+	+	3
J.Z.	M	11.11	106-106-106	LRR	91	?	—	—	6
J.S.	M	9.3	133-125-132	RRL	92	?	+	—	1
R.B.	M	11.4	87- 89- 87	RLR	—	—	+	+	4
F.O.	M	7.0	100- 99- 99	RRR	120	—	+	+	4
J.P.	M	10.7	116-128-124	RLL	71	—	+	+	4
E.E.	M	10.1	115-112-120	RLR	114	+	+	+	4
T.C.	M	10.11	104- 99-101	RRR	111	—	+	+	7
P.C.	M	8.3	104- 94- 99	RRR	88	—	+	+	4
C.B.	M	14.10	116-118-117	RRR	47	—	—	+	3
J.P.	M	10.7	89- 62- 74	RLL	111	—	+	+	2
B.W.	M	11.1	99- 69- 83	RRL	80	—	+	+	1
G.B.	M	14.9	116- 93-106	RRR	—	—	—	+	6
R.S.	M	9.9	91- 78- 83	RRL	—	+	+	—	3
J.R.	F	13.1	103-110-107	RRR	52	—	—	+	6

test and age. However, retardation as measured by this test did not correlate with improvement on drug medication.

Thirty percent of these children have some difficulty with speech (Table I). It is interesting to note that out of three non-improved cases, two have a considerable degree of speech difficulty. It is impossible at this time to draw any conclusions regarding speech difficulty and behavior problems.

By clinical evaluation, the children were divided into three groups based on activity; hyperactive, mixed, and hypoactive.[1] Sixty-four percent of the subjects in the hyperkinetic group (N=11) showed improvement; 100% of the subjects in the mixed group (N=4) showed improvement and 60% of the subjects in the hypokinetic group (N=5) showed improvement.

Brief reports of four children are presented.

Case 1:

Reason for Referral: D. has been a serious behavior problem since he entered the Kansas City schools. Traits and activities that have persisted for considerable time are: crawling on the floor, taking things belonging to others, pulling other's coats and belongings around on the playground, copying other's school work and turning it in as his own, seldom staying in his seat, fussing with other children, doing very little school work, requiring the teacher's constant attention with his questions concerning things that have already been discussed and explained. D. has a ready smile, gracious manners, is alert and responsive to all grown-ups.

Neurological Findings: Child was in treatment for "twisted legs" shortly after birth (casts and braces). Rapidly alternating movements are poorly performed with the left hand and when this is attempted there are definitely some associated movements seen in the right hand.

EEG: Frontal, occipital, and temporal abnormalities.

Dosage: Maximum dosage was 80 mgs. daily (40 at breakfast and 40 at noon). After four months of treatment the child was definitely improved, both at school and at home, with side effects of sleeplessness and less appetite.

Case 2:

Reason for Referral:

Over-aggressive, admits liking to fight, would rather punch children than puncing bag because he likes to see blood, doesn't want to use boxing gloves because "you can't hurt whoever you are fighting," gets along well in the classroom, has all his difficulties on the way to and from school and on playground, will regress to baby talk at times.

Neurological Findings: Prolonged labor and instruments used. Head trauma. Obese. Finger-to-nose test not quite well done with right hand. There are small choreic twitchings noted in the fingers with the hands outstretched. Reflexes are slightly increased in the right arm and right leg.

EEG: Well defined abnormalities in the occipital region.

Dosage: This child tolerated a dose of 200 mgs. daily (100 at breakfast and 100 at noon.) After four and a half months of treatment, he was definitely improved with the side effect of less appetite which was beneficial.

Case 3:

Reason for Referral: Very far below grade level. Plays for attention. He is very negative and irritable at times. C. will ask to talk to the teacher privately, as if upset about something, to keep from doing what he doesn't want to do. C. is very weak. He attaches himself to the moneyed, strong boys and will do anything to be one of them. The principal feels he is afraid to be on the side of the teacher. He drifts with the crowd.

Neurological Findings: Negative.

EEG: Definite abnormalities noted in the occipital area.

Dosage: 90 mgs. (50 at breakfast and 40 at noon). After two and a half months he showed definite improvement without side effects.

Case 4:

Reason for Referral: The boy is beyond parental control and has caused much dissension in the home with brother and sister.

Neurological Findings: On attempting to do fine movements with the left hand there was some clumsiness and on rapidly alternating movements there is some overflow of motor-activity into the right hand. With the patient at rest there are mild choreic twitchings noted in the fingers.

EEG: Normal for age (there are some occipital irregularities without clear pathological significance).

Dosage: 40 mgs. daily (20 mgs. b.i.d.). After one month of treatment the child showed much improvement without side effects.

Discussion

All available evidence points to the fact that methylphenidate has a strong physiological action, which is certainly centrally mediated, and in some cases may have some peripheral components. The exact site of action at this time is unknown, but again the evidence seems to favor thalamic action, cortical action, or both.

We should like to call attention to an effect that seems not to have been hitherto noted. This is the effect that methylphenidate has on immature nervous systems. This effect seems to be one of chemically induced maturation, almost as though one changed an immature, inefficiently functioning nervous system to a mature, efficiently functioning nervous system with goal directed activities.

An interesting fact about the children in this study is that all of them have exhibited in one way or another a great degree of immaturity. At times it has seemed due to obvious brain damage, at other times obvious brain damage could not be demonstrated, and we were forced to conclude that sub-clinical damage existed, a defect which could not be demonstrated by existing diagnostic procedures.

We should like to mention here that another factor might be present. The human being matures, not only in a physiological sense, but in a functional sense. The physiological maturation of the baby's muscles and nervous system permit him to walk at a given physiological age. However along with this must go several other factors which are also components of maturity. One of these factors is the desire to walk. A desire to walk suggests a goal-directed activity, and goal-directed activity in itself suggests a certain degree of cortical maturity.

The children we have seen in this study have impressed us as being cortically immature in the sense that they could not pursue a logical course of goal-directed activity, could not accustom themselves to orderly precise habits, could not tolerate frustration, and could not function efficiently in the pursuit of their daily duties.

The administration of methylphenidate to these children resulted in a decrease in the absolute amount of motoric activity but in an increase in the amount of motoric activity devoted to goal-directed behavior. Attention span was increased, and the child could keep his attention focused on the task at hand. At the same time their general situation was bettered because they were not indulging in antisocial motoric activity, they were producing more social activity, and they were better accepted by their peer groups, their teachers, and their parents. It was interesting that in many cases their sleeping habits improved, even though in some cases sleeplessness appeared as an undesirable side effect.

Conclusion

If we accept the possibility of organic basis for behavior disorders, our pilot study of 20 children suggests that methylphenidate has several effects which reinforce and enhance each other. The first of these is a stimulating effect on a central nervous system which may or may not be accompanied by peripheral components. The second of these effects to which we would particularly like to call attention is an effect on the total functioning of the nervous system and the cortex in particular. This, we describe as a "maturing" effect, or a state of increased efficiency in total brain functioning. This drug seems to be efficacious in the treatment of behavior disorders in children.

Summary

1. A review of current concepts on organic basis of behavior disorders is presented.

2. The results of a pilot study of the use of methylphenidate in behavior disorders is briefly demonstrated.

3. Ritalin proved efficacious in 15 out of 20 behavior disturbed children. Side effects were minimal.

4. The conclusion is drawn that methylphenidate acts on the cortex and produces goal-directed, coordinated behavior.

Authors' Note: The Ritalin® used in this study was obtained through the courtesy of the CIBA Pharmaceutical Company, Summit, New Jersey.

The behavioral rating scale was used by arrangement with Harold F. Burks, Ph.D., Altadena, Calif.

BIBLIOGRAPHY

1. Kirkpatrick, M., et al.: A Redefinition of the Behavior Disorder Concept. Paper presented at the *114 Meeting of A.P.A.*, San Francisco, May 1958.
2. Knobel, M.: A Syndromic Approach to "Acting-out" Children. *Dis. Nerv. Syst.*, XX, 1(2):80; Feb. 1959.
3. Kahn, E., and Cohen, L. M.: Organic Driveness, a Brain Syndrome and an Experience. *N. Eng. J. Med.*, 210:748, April 1934.
4. Livingston, R. B.: Some Brain Stem Mechanisms Relating to Psychosomatic Functions. *Psychosom. Med.*, 17:347, Sept.-Oct. 1955.
5. Livingston, R. B., and Worden, F. G.: Some Neurophysiological Contributions to Internal Medicine. *Stanford Med. Bull.*, 13:194, May 1955.
6. MacLean, P. D.: The Limbic System ("Visceral Brain") in Relation to Central Gray and Reticulum of the Brain Stem. Evidence of Interdependence in Emotional Processes. *Psychosom. Med.*, 17:355, Sept.-Oct. 1955.
7. Malamud, N.: Psychiatric Symptoms and the Limbic Lobe. *Bull. Los Angeles. Neurol. Soc.*, 22(3):131, September 1957.
8. Fulton, J. F.: Frontal Lobotomy and Affective Behavior. *W. W. Norton and Co.*, New York, 1951.
9. Penfield, W., and Rasmussen, T The Cerebral Cortex of Man. *McMillan Co.*, N. Y., 1950.
10. Freeman, W., and Watts, J. W.: Psychosurgery. *Ch. C. Thomas*, Springfield, Ill., 1950.
11. Brock, S.: Dynamic Mechanisms Underlying Some Forms of Cerebral Dysfunction. *Am. J. Psychiat.*, 105:246, Oct. 1948.
12. Dusser de Barenne, J. G., and McCulloch, W. S.: Suppression of Motor Response Obtained from Area 46 by Stimulation of Area 45. *J. Neurophysiol.*, 3:311; 1941.
13. Gibbs, E. L., Gibbs, B. A., and Fuster, F. A.: Psychomotor Epilepsy. *Arch. Neurol. Psychiat.*, 60:331, 1948.
14. DeJong, R. N.: Psychomotor or Temporal Lobe Epilepsy. *Neurology*, 7:1, Jan. 1957.
15. Bender, L.: Psychological Problems of Children with Organic Disease. *Am. J. Orthopsychiat.*, 19:404, July 1949.
16. Bender, L.: Organic Brain Conditions Producing Behavior Disturbances, a Clinical Survey of Encephalitis, Burn Encephalopathy and the Traumatic States (in Modern Trends in Child Psychiatry, W. D. C. Lewis and B. L. Pacella, Eds. *Int. Univ. Press*, New York, 1945).
17. Goldstein, K.: The Organism. *Amer. Book Co.*, New York, 1939.
18. Werner, H.: Thought Disturbance with Reference to Figure Background Impairment in Biological Intelligence. *Trans. Am. Neurol. Assn.* Brain-Injured Children. *Confinia. Neurol.*, 9:255; 1949.
19. Werner, H., and Weir, A.: The Figure-Ground Syndrome in the Brain-Injured Child. *Intern. Record of Med. and Gen. Pract. Clinics.*, 162:362, June 1956.
20. Clark, Jr., L. C.: The Chemistry of Human Behavior. *Am. J. Orthopsychiat.*, 18:140, Jan. 1948.
21. Ashby, W.: An Approach to the Solution of Mental Dysfunction Through Brain Enzyme Studies. *Am. J. Psychiat.*, 106:491; Jan. 1950.
22. Rinkel, M., and Solomon, H. C.: Chemical Theories of Psychosis. *J. Clin. Exp. Psychopathol.*, 18(4):323; Dec. 1957.
23. Halstead, W. C., and Shure, G.: Further Evidence for a Frontal Lobe Component in Human 1954.
24. Eisenberg, L.: Psychiatric Implications of Brain Damage in Children. *Psychiat. Quart.*, 31(1):72, Jan. 1957.
25. Masserman, J. H., and Pechtel, C.: How Brain Lesions Affect Normal and Neurotic Behavior, An Experimental Approach. *Am. J. Psychiat.*, 112:865; May 1956.
26. Magoun, H. W.: An Ascending Reticular Activating System in the Brain Stem. *Arch. Neurol. Psychiat.*, 67:145; 1952.
27. Jasper, H., et al.: Corticofugal Projections to the Brain Stem. *Arch. Neurol. Psychiat.*, 67:155; 1952.
28. Spiegel, E. A., et al.: The Central Mechanism of the Emotions (Experiences with Circumscribed Thalamic Lesions). *Am. J. Psychiat.*, 108:426, 1951.
29. Laufer, M. W., Denhoff, E., and Solomons, G.: Hyperkinetic Impulse Disorder in Children's Behavior Problems. *Psychosom. Med.*, 19:38, Jan.-Feb. 1957.
30. Laufer, M. W., and Denhoff, E.: Hyperkinetic Behavior Syndrome in Children. *J. of Pediatr.*, 50:463, April 1957.
31. Bradley, C.: The Behavior of Children Receiving Benzedrine. *Am. J. Psychiat.*, 94:577; 1937.
32. Bradley, C., and Bowen, M.: Amphetamine (Benzedrine) Therapy of Children's Behavior Disorder. *Am. J. Orthopsychiat.*, 11:92; 1941.
33. Burks, H. F.: The Effects of Amphetamine Therapy in Children with a Cortex Injury Versus Those with a Mid-brain Injury. Unpublished paper presented at the *California Educational Research Association*, Santa Barbara, California, March 1957.
34. Meir, R., Gross, F., and Tripod, J.: Ritaline, eine neuartige synthetische Verbindung mit spezifischer zentralerrengender Wirkungskomponente. *Klin. Wschr.*, 32:445, May 1954.
35. Carter, C. H.: The Effects of Reserpine and Methyl-phenidylacetate (Ritalin) in Mental Defectives, Spastics and Epileptics. *Psychiat. Res. Reports*, 44-48, No. 4, 1956.
36. Heiss, R., et al.: Verber psychische Wirkungen eines neuartigen Psychotonikums Medizinische, 5:260, 1956 (Abstract).
37. Carter, C. H., and Maley, M. C.: Parenteral Use of Methylphenidate (Ritalin). *Dis. Nerv. Syst.*, 18:146; April 1957.
38. Hartert, Dietrich, Browne-Mayers, Albert N.: The Use of Methylphenidate (Ritalin) in Alcoholism. *J.A.M.A.*, 116:1982, April 19, 1958.
39. Maxwell, R. A., et al.: Antihypertensive Effects of the Central Nervous Stimulant Methylphenidate. *Arch. Internat. Pharmacodyn.*, 112:26, Oct. 1957.
40. Plumer, A. J., Maxwell, R. A., and Earl, A. E.: Some Pharmacological Inter-Relationships Beween Methyl-phenidate (Ritalin) and Reserpine. *Am. J. M. Sc.*, 233: 719, June 1957.
41. Ehrmantraut, W. R., et al.: Influence of Proma-

zine and Methylphenidate on Cerebral Hemodynamics and Metabolism. *Arch. Int. Med.*, 100:66, July 1957.
42. Cole, J., Glees, P.: Ritalin as an Antagonist to Reserpine in Monkeys. *The Lancet*, p. 338; March 24, 1956.
43. Cole, J., and Glees, P.: Some Effects of Methylphenidate (Ritalin) and Amphetamine on Normal and Leucotomized Monkeys. *J. Ment. Sc.*, 103:406; April 1957.
44. Burks, H. F.: A Study of the Organic Basis for Behavior Deviations in School Children. Unpublished Doctoral Dissertation at the University of Southern California; May 1955.

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Incidence of Fourteen and Six Per Second Positive Spike Discharges in Routine Sleeping EEG's

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In 1000 consecutive routine sleeping electroencephalograms taken in the laboratory of a 350 bed private hospital,* 139 records were found showing fourteen and six per second positive spike activity. This activity has been considered to be of subcortical origin, probably from the thalamus or hypothalamus.[1]

Examples of this EEG pattern are shown below to clearly indicate the activity under discussion:

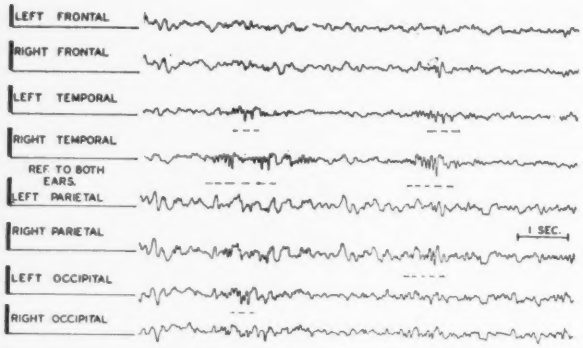

Figure 1.

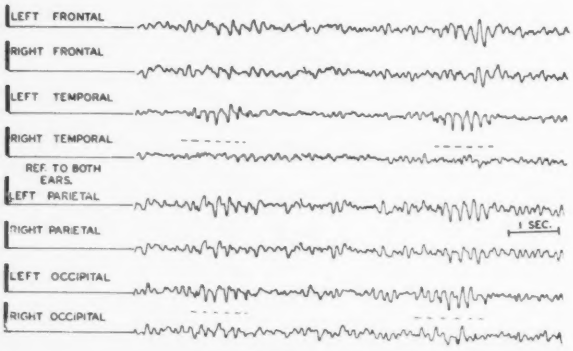

Figure 2.

*Decatur and Macon County Hospital, Decatur, Ill.

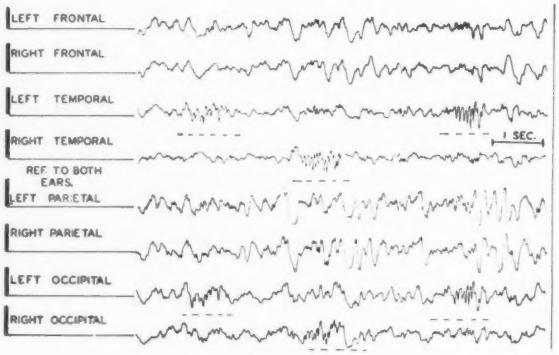

Figure 3.

The lead placement used was as follows:

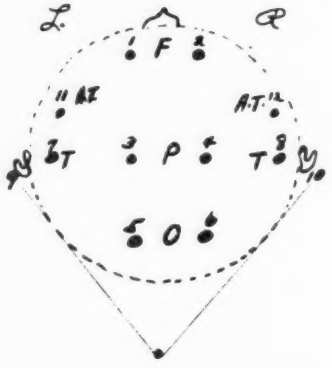

Figure 4.

Tracings were taken on a Model III Grass Electroencephalograph. The ears were connected and used as a common reference electrode. Bi-polar recordings were also made. The records were all run with the patient both awake and asleep. (Sleep was spontaneous or induced by oral Seconal.)

All patients were referred by their private physicians because of their various symptoms, or a head injury or serious accident. Of the 139 records, 76 patients had suffered

significant head injury. There were 40 cases without suspected or known etiology. Of the 139 cases 54 or 38% were in the 10-19 age group and 35, or 25% were 20 to 29 years old.

AGE DISTRIBUTION

CASES OF 14 AND 6

Age			Distribution of all 1000 cases	
0-4	4	2.8%	96	9.6%
5-9	19	13.6%	101	10.1%
10-19	54	38.8%	184	18.4%
20-29	35	25.2%	170	17.0%
30-39	18	12.9%	164	16.4%
40-49	7	5.0%	120	12.0%
50-59	2	1.4%	76	7.6%
Over 59	0	.0	89	8.9%
	139		1000	

Symptomatology associated with this finding in the records included attacks of headache in 63 patients, fainting in 17, attacks of vertigo in 18, and grand mal seizures in 14. The remainder are listed in the following table:

	Cases
Headache	63
Attacks of vertigo	18
Grand mal seizures	14
Fainting	17
Nausea	13
Visual disturbance	10
Attacks of inability to talk	6
Staring spells	4
Uncontrollable crying	3
Vomiting	4
Sleeping	4
Lapses of attention	2
Focal numbness	1
Slurring of speech	1
Abdominal pain	1
Sleep-walking	1
Grimacing	1
No symptoms	9

(Many patients had more than one symptom, so no total is given.)

Etiology—the following is a list of associated findings which may or may not be significant as etiological factors:

	Cases
Head injury	77
Anoxia at birth	6
Abscess of ear (with mastoid infection)	2
Severe pneumonia or scarlet fever	4
Chorea (acute)	1
High fever (106 or above)	*
Cerebral palsy	2
Hodgkins disease (intracranial spread)	1
Meningitis	1
Craniopharyngioma	1

An attempt was made to follow these patients at least one year after the records, to determine the success of treatment. Eighty-three, or 59.7% of the 139 were reported on, and of this number 38 were taking medication with improvement. Medication included Dilantin, phenobarbital, Mysoline and Mesantoin.

Conclusion

In this study of minor seizures and the associated EEG findings it is noteworthy that 13.9% of the patients had the finding of 14 and 6 per second positive spike activity in their records. This would have been missed in most cases if sleep had not been obtained. It was most readily detected in the drowsy and light sleep phases. Only 38 of the 139 patients were found to be taking medication a year after the record. This is explained by the fact that the symptoms accompanying the EEG findings in a large percentage of the patients were not sufficiently serious or disturbing to make them willing to take regular medication over a long period of time. The correlation of this EEG pattern with the clinical symptoms has been of definite value in helping the clinician to treat and explain many otherwise odd and peculiar subjective symptoms.

BIBLIOGRAPHY

1. Gibbs and Gibbs: Atlas of Electroencephalography, Vol. II, pages 329 to 345.

Aids in Diagnosis of Epilepsy in Servicemen

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The difficulty in establishing a diagnosis of epilepsy in spite of the frequency of this disease and its long history in medical annals is well recognized. Often the classic symptomatology takes on modifications and permutations. Yet it is of greatest importance to diagnose the conditions as many beneficial therapeutic means are available. Furthermore the danger to property and to other persons due to an epileptic seizure is intensified in the armed forces, especially since a spell may occur in situations of hazardous duty. On the other hand to place a label of epilepsy erroneously has many unfortunate sequelae particularly from a legal and psychiatric viewpoint. For these reasons it is important to attempt to find ways to aid in arriving at a correct diagnosis.

There is abundance of literature which links some cases of enuresis to epilepsy. This evidence is cited in previous papers[2-7] where it was observed that many enuretic sailors had a family history of epilepsy and somnambulism as well as enuresis. Indeed some enuretics had a past history of treatment for epilepsy Compared to a control group of non-enuretics, the enuretic Naval recruit was apparent statistically because of abnormal brain waves. It was noted also that although the young adult male enuretic had a plethora of psychiatric problems rooted in disturbed psychodynamics, psychologic testing is suggestive of organic deficit.

The object of the present investigation was to determine whether certain items in a medical history are found often enough in epileptics to be of use in suspecting this diagnosis amongst service personnel. Some of the research implications of such item associations have been discussed elsewhere.[4,6] In the present study it was found that in servicemen epilepsy is associated clinically with a family and past history of enuresis and a present history of enuresis and sleepwalking. These men are nervous and easily fatigued.

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The opinions or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

Method and Material

Interviews (by HHL) and electroencephalographs were obtained at the Great Lakes Naval Hospital on 50 in-patients consecutively diagnosed as epileptic and on 50 in-patients diagnosed with non-epileptic, non-neuropsychiatric disorders. An effort was made to match the composition of the groups. Thus the experimental group consisted of 48 whites and 2 negroes with age range of 17-41, average being 19.9 years; ratings included 32 Naval recruits, 7 enlisted soldiers, 7 enlisted sailors, 1 enlisted airman, 2 enlisted marines, 1 Naval officer; marital status was 43 single, 1 divorced and 6 married. The control group consisted of 48 whites, 2 negroes with age range of 17-36, average being 20.7 years; ratings included 32 Naval recruits, 5 enlisted soldiers, 9 enlisted sailors, 1 enlisted airman, 2 enlisted marines, 1 Naval officer; marital status was 44 single, 1 divorced, 5 married.

All 100 subjects were given EEG's and questioned in regard to present, past and family history of enuresis, sleepwalking and epilepsy. Family was defined to include only "blood" relations: parents, siblings, grandparents, aunts, uncles, nephews, nieces, first cousins. Enuresis was defined in this project to mean persistent trouble with bedwetting after age 5. A history of one sleepwalking episode was considered positive in this investigation. The men were asked, too, about a personal history of nervousness, tremors, insomnia, fatigue, prolonged headaches, syncopal spells and severe head injury. This personal data was adopted from Rossen and Gordon[6] but qualified by Gibbs and Wenger's[5] criteria for a severe head injury. Thus a severe head injury meant the man could give a history of having had a trauma followed by loss of consciousness for over one hour, bloody spinal fluid, brain laceration, compound fracture, subdural or extradural hematoma.

The men in the experimental group were

diagnosed as epileptic only after presenting a clinical history of recurrent seizures which satisfied the experience of the investigator as representing epilepsy. All these cases had to have abnormal brain waves. In most instances seizures were observed by competent medical personnel. Usually social service reports from the man's home town verified the subject's account and knowledge of his spells. In most cases clinical improvement followed the use of anticonvulsant medication. The epileptics were queried concerning aurae, prodromal symptoms, knowledge of loss of consciousness, tongue biting, incontinence, post ictal confusion, post ictal sleep, post ictal headache and convulsions. By history many men confessed a diagnostic workup and treatment for epilepsy.

In the control group there were 22 men who were diagnosed as having bronchopneumonia. Nine men had fractures. Two men each had penicillin reactions, hip dislocations and internal derangement of the knee. There was one man with each of the following ailments: diabetes mellitus, diabetes insipidus, chronic seasickness, paralysis of median nerve, duodenal ulcer, osteomyelitis, heart murmur, hernia repair, atypical pneumonia, medical observation, surgical observation, genito-urinary observation and loose bodies in the left ankle.

Results

Tables 1 and 2 summarize the material from this study. It is of statistical significance that about half of the epileptics consider themselves nervous and give a family and past history of enuresis (in fact one-fifth of the experimental group continues to bedwet). About one-third of the epileptics are troubled by fatigue and know of a family history of epilepsy. About one in six of the experimental group is a sleepwalker.

A great majority of the epileptics which are seen in a service in-patient ward suffer from grand mal seizures. These servicemen almost always know that they are epileptic and can describe their spells as leading to unconsciousness and convulsions after specific prodromal symptoms. Most have bit their tongue and have had post ictal confusion, sleepiness and headache. However, relatively few men are able to tell of an aura or incontinence associated with the convulsion. More epileptic servicemen knew of a family and past history of enuresis than of an aura or incontinence as part of their seizure pattern. A family history of epilepsy was found about as often as knowledge of aura or incontinence.

Statistically, the control group was just as likely as the experimental group to give a past and family history of sleepwalking. The groups were similar so far as a history of severe head injuries, syncopal spells, prolonged headaches, tremor and insomnia. Ten of the control group and fifty of the experimental group had abnormal brain waves. However, the control group abnormalities were all min-

TABLE 1

Interviews With 50 Epileptics and 50 Non-Epileptics

Interview Item	Epileptics N=50	Non-epileptics N=50	χ^2	P	Interpretation
Family History of Enuresis	25 (50%)	11 (22%)	7.33	<0.01	highly significant
Past History of Enuresis	26 (52%)	12 (24%)	7.17	<0.01	highly significant
Present History of Enuresis	10 (20%)	0 (0%)	9.00	<0.01	highly significant
Family History of Epilepsy	16 (32%)	0 (0%)	16.74	<0.001	very highly significant
Consider Themselves Nervous	23 (46%)	7 (14%)	10.71	<0.01	highly significant
Troubled by Fatigue	14 (28%)	4 (0%)	5.48	<0.02	significant
Present History of Sleepwalking	*8 (16%)	0 (0%)	6.98	<0.01	trend toward significance
Past History of Sleepwalking	12 (24%)	5 (10%)	2.55	<0.10	not significant
Family History of Sleepwalking	*6 (12%)	4 (8%)	2.77	>0.10	not significant
History of Severe Head Injuries	*9 (18%)	4 (8%)	0.70	>0.10	not significant
History of Syncopal Spells	10 (20%)	3 (6%)	3.18	<0.10	not significant
History of Prolonged Headaches	12 (24%)	5 (10%)	2.55	<0.10	not significant
History of Tremors	12 (24%)	5 (10%)	2.55	<0.10	not significant
History of Troubles with Insomnia	13 (26%)	5 (10%)	3.31	<0.10	not significant

*Sample too small for confident analysis.

TABLE 2

Epilepsy in 50 Servicemen

Could report aura	16
Could report prodromal symptoms	33
Knew of history of loss of consciousness	49
Knew of history of tongue biting	31
Knew of history of incontinence	14
Knew of history of post ictal confusion	45
Knew of history of post ictal sleep	41
Knew of history of post ictal headaches	32
Knew of history of convulsions	44
Knew of history of epilepsy	40
Types of Epilepsy	
Grand mal	45
Petit mal	9
Psychomotor	2
Jacksonian	2
Focal	1
Post traumatic	1
Combination	8

imal in comparison to the more frequent gross abnormality found in an epileptic.

Of the epileptics 44 were discharged from service subsequent to diagnosis; epileptics who were stabilized by medication were permitted to return to duty. Of the controls 47 returned to duty. One control was given an administrative discharge after it was discovered that he was homosexual. In two controls disposition was not established.

Discussion

Since the ultimate fate of most epileptics in the armed forces is discharge or a limited duty, it is important to be aware of this diagnosis so that it can be detected and disposition arranged as early as possible. This would avoid costly but wasted training effort by the military. It would decrease, also, the adjustment problems of the individual. This study suggests that a serviceman with a family, past or present history of enuresis might be suspect as a potential epileptic. The problem arises immediately whether these men had nocturnal epilepsy with incontinence. This question is of more theoretic than clinical importance since in all cases in this series the patient believed himself to have been bedwetting. Thus there were no injuries, subjective evidence or reports from family observers to indicate to the person that epilepsy was involved. To the questioning physician, therefore, the suspected epileptic would report that he has or had trouble with bedwetting. The suspect is likely, too, to admit nervousness and easy fatigue. These complaints are general and are found in many patients seen on a neuropsychiatric service. But a high index of suspicion of epilepsy should be maintained if these complaints are found in a man who admits also of bedwetting and sleepwalking problems. Such a combination of complaints is not unusual, particularly on the medical screening sheets of incoming recruits who have arrived at their first duty station.

It was surprising to discover that 40 of the 50 epileptics had a prior history of epilepsy. The explanation might be that it was necessary to conceal or minimize the history of "blackout," in order to gain admission to the service. Another report will detail some of the emotional stresses peculiar to military duty which seem to precipitate a dormant epilepsy. Yet there was some inclination in these patients to believe that their epilepsy was a past illness. They pointed out that they had been able to abandon successfully, for one or more years, the treatment which had been prescribed. There were 22 men in this category. Some of this group had relinquished anticonvulsants ten years prior to military service when suddenly, under the pressures of recruit training or service adjustment, overt epilepsy reappeared.

Since 40 of 50 in the experimental group admitted a past history of epilepsy it may be assumed that this group had greater personal and external pressure to find out about a family history of epilepsy. Nevertheless the increased family history of epilepsy is consistent with many previous studies. There is an application of this material since it means the military doctor can ask about a past history of epilepsy rather than assume it to be absent because the subject already is in service. The past history of bedwetting problems, however, will be found more frequently than knowledge of incontinence and aura.

A research design which obligates an abnormal brain wave as a criterion for admission to the experimental group helps force an overwhelming statistical significance for that criterion ($x^2=63.37$, $P<0.001$). The ten abnormal brain waves in the control group were qualitatively much less severe than

those of the experimental group. Finding 20% abnormal tracings in a population with an assortment of known pathophysiology does not seem beyond the boundaries of expectation.[6]

Of 100 subjects in this project, only eight admitted to persistent somnambulism. All eight of these men were epileptics. Sleepwalkers come to medical attention, in the service, much less frequently than bedwetters. Yet, when they do come for medical observation, they too have many associations with bedwetters as far as history of enuresis, abnormal brain waves and chronic genito-urinary complaints.[2-5] It may be that all young adult sleepwalkers should be given electroencephalographs.

Due to the secondary gains from somnambulism (permanent shore duty or discharge from the service) and the emotional aggravation of sleepwalking in the Navy, it has been difficult to assess the therapeutic value of Dilantin in oil on sleepwalkers. We theorize that if sleepwalking in young adults might be related to epilepsy, an anticonvulsant with slower release through the night might be effective in controlling the disturbance. At any rate a serviceman who complains of sleepwalking but who warrants retention in the service, should be evaluated for possible epilepsy.

This study has pointed up the fact that in young adult males who are in otherwise good health, a doctor must be suspicious of epilepsy if the patient persists with symptomatic immaturity habits of enuresis and sleepwalking. Also, when establishing a diagnosis of epilepsy a family and past history of enuresis are perhaps as likely to be obtained as a history of aura or incontinence.

Summary

The diagnosis of epilepsy often is difficult. All doctors appreciate the need for early, accurate diagnosis so that treatment may be started. In the military service it was found that many enuretics and sleepwalkers showed abnormal brain waves, phenomena of dejavu, "organicity" on psychological testing and family, past and present histories of both enuresis and sleepwalking. Often these men had positive family and personal histories of epilepsy.

In the present study 50 epileptics and 50 non-epileptics were studied by means of electroencephalographs and interviews designed to learn about associations with epilepsy, enuresis, somnambulism and specified neuropsychiatric complaints. It was of statistical significance that the epileptics considered themselves nervous, easily fatigued and they had family, past and present histories of enuresis. It was significant too that these men had a family history of epilepsy. The only subjects in this study with persistent sleepwalking were in the experimental group.

It is concluded that amongst "healthy" adult males, persistent enuresis and/or somnambulism should arouse suspicion of epilepsy. A family and past history of enuresis may be found more frequently in known epileptics than knowledge of an aura or incontinence during an attack. A family or past history of enuresis may be found as frequently in known epileptics as a family history of epilepsy.

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BIBLIOGRAPHY

1. Gibbs, F. A., and Wenger, W. R.: The Electroencephalogram in Post Traumatic Epilepsy. *Am. J. Psychiat.*, 1002 (1944), 738-744.
2. Pierce, C. M., and Lipcon, H. H.: Somnambulism: Electroencephalographic and Related Findings. *U.S. Armed Forces M. J.*, 7 (1956), pp. 1419-1426.
3. Pierce, C. M., and Lipcon, H. H.: The Clinical Relationship of Enuresia to Sleepwalking and Epilepsy. *Arch. Neurol. and Psychiat.*, 76 (1956), pp. 310-316.
4. Pierce, C. M., Lipcon, H. H., McLary, J. H., and Noble, H. F.: Enuresis: Clinical, Laboratory and Electroencephalographic Studies. *U.S. Armed Forces M. J.*, 7 (1956), pp. 208-219.
5. Pierce, C. M., Lipcon, H. H., McLary, J. H., and Noble, H. F.: Enuresis: Psychiatric Interview Studies. *U.S. Armed Forces M. J.*, 7 (1956), 1265.
6. Rossen, R., Gordon, M.: Electroencephalographic Findings in a Naval 'Control' Group of 259 Men. *Dis. Nerv. Syst.*, R AVTDGQ, 373-378.

Theoretical Considerations in Parkinsonism Induced by Tranquilizing Drugs

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The induction of parkinsonism by chlorpromazine and reserpine has been widely observed but little understood. An experience[1] with a unique parkinsonism in which psychic factors were etiologically crucial, and in which the parkinsonian akinesia clearly served to control an enormously threatening eruption of hate, engendered curiosity about possible psychologic factors in the pathogenesis of the drug-induced syndrome.

So far as we are aware, our case is the only one so far reported in which a *chronic* parkinsonian state appeared to have a psychogenic basis. Grinker and Spiegel[2] had previously described acute, transient parkinsonian reactions in a few cases of combat neurosis during the North African campaign (World War II). It does not seem *a priori* at all surprising that that a parkinsonian akinesia *might* arise on a psychogenic basis when one considers the role which Papez[3] ascribes to the basal ganglia and their connections with the lower levels of the motor apparatus:

"Control of the more elaborate but stereotyped inhibitions, postures, attitudes and movements related to the basic needs of the organism."

Indeed, Cooper,[4] a neuro-surgeon, asks of parkinsonism generally:

"What are the psychological components of the disease? *Are many cases actually psychogenic?*"

Mettler[5] remarks that the prevailing conception of the late 19th century assigned parkinsonism to the category of "neuroses" such as neurasthenia and hysteria because pathologists had failed to discover characteristic lesions in the brain. S. A. K. Wilson, who described "progressive lenticular degeneration," helped initiate a shift toward an organic conception.

A considerable literature on the characterology of parkinsonism (C. D. Camp, 1913; Smith Ely Jelliffe, 1927, 1940; Buerger and Mayer-Gross, 1928; E. Stengel, 1935; and G. Booth, 1948) bears testimony to the contribution of psychic factors in cases with obvious organic impairment. Since there can be no doubt, descriptively speaking, that Grinker's and Spiegel's cases as well as our own are properly designated instances of Parkinson's "syndrome," it would appear justified to add a "psychogenic" category to the existing catalogue of underlying disease processes. The drug-induced cases would seem to present difficulty as to classification in this respect, depending upon the theory adopted as to their pathogenesis. If, for example, one regards these cases solely as instances of a reversible pharmacologic effect on the higher brain stem, they would necessarily constitute a separate etiologic category. Unfortunately, pathologic studies are of no help in deciding this issue. Kinross-Wright[6] mentions a fatality from chlorpromazine in which lesions of the globus pallidus and subthalamic nuclei of Luys were demonstrated although the patient had exhibited neither symptoms of parkinsonism nor of hemiballismus. Moore[7] mentions a fatality in which some parkinsonian manifestations (tremor and dysarthria) preceded death by three days. No lesions characteristic of parkinsonism were found.

No doubt among the various effects of chlorpromazine and reserpine none seems at first glance so capable as parkinsonism of a purely neuropharmacologic explanation (without any necessity of considering contributions by the individual's character structure). A theory has been offered by Himwich & Rinaldi,[8] based indirectly upon EEG studies in cats and rabbits which indicated that all doses of reserpine and larger doses of chlorpromazine excited the "reticular activating system." The authors compare this chemical excitation to what they conceive as the mechanism of production of parkinsonism generally: "liberation of the reticular activating system from cephalad control due to lesions in the basal ganglia and substantia nigra."

Curiosity prompted a review of the relevant neurologic and neurophysiologic litera-

ture upon which this theory was said to be based. An impression was gained that the neural mechanisms of drug-parkinsonism were no better understood than those of "spontaneous" parkinsonism. It then seemed desirable to consider possible means of interaction between neural and psychic factors. It will be the task of this communication to explore this border-line territory and to develop a hypothesis in regard to the possible mechanism of genesis of drug-parkinsonism relating both aspects. The neural side of the problem will be discussed first.

Neurophysiology

Himwich and Rinaldi[8] concern themselves primarily with the manner in which chlorpromazine and reserpine effect the "mesodiencephalic alerting system" (MDAS) of cats and rabbits. They subdivide the mesodiencephalic alerting system for their purpose into the "reticular formation" of Moruzzi and Magoun[9] and the "thalamic diffuse cortical projection system" of Jasper.[10] They regard drug-induced parkinsonism as a by-product of overstimulation of the former. However, the authors treat the R. F. as a single entity, omitting the consideration that it is divided into a medullary portion which *inhibits* and a pontine-diencephalic portion which *facilitates* cortically induced movement. They regard the activity of the R. F. as varying simply along an axis of inhibition-stimulation. They state that the effectiveness of anti-parkinson drugs varies with the degree to which they "block the MDAS, mimicking the central action of atropine." (Similarly, anxiety is correlated by them with overactivity of the MDAS as indicated by fast, poorly organized alpha rhythm.)

The conception of parkinsonism generally as due to "liberation" of the R. F. from inhibition by the basal ganglia is a leftover from Bucy's[11] unconfirmed theory of the "4S circuit" (cortex > caudate N. > pallidum > N. ventrolateralis > cortex), which was alleged to have a suppressor effect on pyramidal activity. This action was said to be lost when pallidal degeneration broke the suppressor circuit, liberating a hypersynchronized pyramidal discharge. Evidence against this theory is summarized by Cooper.[4]

Mettler[5] states that experimental pallidal lesions in animals result in "a veritable melee of irregular results which defy simple analysis." Spiegel and Wycis et al.[18] as well as Cooper[4] and Davison[59] consider many paradoxical features presented by both experimental and pathological conditions of various portions of the pallidum which make any simple explanation of the role of this structure in the production of parkinsonian manifestations very shaky. It appears that parkinsonism is in no wise explainable on the basis of simple underactivity or overactivity of either the R. F. or the pallidum. Cooper[4] modestly states that the unknown aspects of parkinsonism exceed the known, and that the greatest progress has been the doubt cast upon older ideas.

The interesting results of Himwich and Rinaldi[8] do, however, suggest an alternative explanation. If the drugs stimulate the R. F. but depress the hypothalamus, is it not possible that these two regions might *be out of phase?* The "stimulated" R. F. does indeed appear to facilitate EEG arousal reactions, but might this not be on a basis of "free-wheeling"? If the R. F. is, as it were, out of gear, then its alleged hyperactivity (as indicated solely by the criterion of the EEG) might not be adequate to explain the phenomena of parkinsonism even on the theoretical basis proposed by the authors.

Another attempt to explain thorazine-induced parkinsonism in chemical terms is that of Azima and Richman.[20] In a study as yet unconfirmed these authors claim to have found an alteration of copper metabolism in chlorpromazine treated cases. They started with the preconception that such an anomaly would facilitate explanation of drug-induced parkinsonism in terms of Wilson's hepatolenticular degeneration. Little more than a sketchy analogy could be drawn, one which presented several inconsistencies and left many unanswered questions. No general agreement exists among biochemists as to the elevated or depressed status of plasma copper in Wilson's disease, so that the finding of an elevated value in the drug cases is not conclusive. Also, none of the drug-Parkinson cases showed any evidence of liver damage. Further, of 25 cases studied, only 12 showed abnormally high copper values

and only five of these developed an extrapyramidal disorder. The liver-damaged cases showed pathologic changes of cholangitis while those of Wilson's disease are parenchymal, and it was necessary to postulate that further lapse of time might produce parenchymal damage from the drug. However, this theory does not explain parkinsonism due to reserpine. From a purely clinical viewpoint, it seems scarcely possible that the eminently reversible drug cases could be etiologically related to the relentlessly progressive picture of Wilson's disease. If, indeed, the copper anomaly is confirmed by further studies, it will have to be regarded as an epiphenomenon of no etiologic significance.

Lehman[21] has envisioned chlorpromazine as depressing the diencephalic centers in such a way that anxiety is reduced, and he coined the phrase "pharmacologic mesencephalotomy" to epitomize this effect. He conceives drug-parkinsonism as due to extension of the drug effect too far cephalad.

Is it possible that these excursions into realms of "pure" neuropharmacology have unduly neglected consideration of possible psychologic factors in these cases? Neurologists despair of explaining all the phenomena of parkinsonism in terms solely of their own discipline. One might consider the possibility of viewing this syndrome as a complex reaction pattern in which both neurologic and characterologic factors play interdigitating roles—which might well vary from case to case in relative importance. The same comment applies to many "neurologic" diseases. The "psychosomatic approach" to organic diseases of the neuromuscular apparatus is of particular interest psychiatrically because one deals here with impairments of the executive organs of the ego itself. Hollos' and Ferenczi's work on general paresis is a classic in this field. Jelliffe may be said to have done for parkinsonism what these authors did for paresis.

Psychologic Aspects

A recent publication of Sarwer-Foner and Ogle[22] records a pioneering attempt to correlate the effects of chlorpromazine and reserpine with the vagaries of individual psychopathology. The authors state: "These drugs are not *specific agents* but *symptomatic drugs*. Both *hold down* the patient physically. If the patient does badly, the physiological effect threatens him." And again: "The nosologic entity produced by the drug is not a function of the specific action of the drug but a response of the patient and his total assets to the removal of one of his important defenses—activity. It is naive to attribute the effect to some possible vague specific action of these agents on the brain stem." The authors describe several types in whom physical activity is a highly necessary defense and to whom the immobilizing effects of these drugs was an added stress aggravating the illness.

Unpublished observations in the same vein by R. Schmiedeck,[23] indicate that schizophrenic patients with a strong tendency to "act out" (relieve inner tension by immediate physical action), experience an increase rather than a decrease of anxiety under the motoric inhibition of chlorpromazine. That adult patients with similar "acting out" tendencies due to so-called "character disorders" are made increasingly anxious by chlorpromazine is well known. Disturbed, hyperactive children exhibit similar behavior but the diagnostic and prognostic significance is quite different. Freed[24] reports good results in controlling anxiety and hyperkinesis in such disturbed children with chlorpromazine, a result which contrasts with that mentioned above in similarly behaving adults. (This contrast will be further developed below.) Freed[24] makes bold to suggest that patients with chlorpromazine-induced parkinsonism might have a "psychic vulnerability exposed by the drug effect."

Numerous reports[25-32] of psychiatric improvement in a significant number of cases coincidental with the appearance of extrapyramidal symptoms further suggested that the induced parkinsonism might sometimes be a therapeutic asset. Sainz[25] states that extrapyramidal effects, "far from being complications, are closely related to the drug's (chlorpromazine) effectiveness." He postulates that the drug, through an effect on the "glio-pallidal centers," produces a "variable reduction in psychomotility" which may simply progress so far that it "assumes parkinsonian proportions." This concept of "reduced motility" as an *anlage* of drug-in-

duced parkinsonism is novel and arresting.

Curiously enough, paralysis agitans (parkinsonism due to organic disease of the basal ganglia) has long been thought to confer upon its victims protection against a number of other dread diseases which psychosomaticists are today attempting to correlate with the patients' self concepts, styles of life, etc. For example, Doshay[33] suggests that patients suffering from it are less likely than others to develop cancers, hypertension or tuberculosis. Staehelin[34] remarks that it was observed 30 years ago that chronic schizophrenics who developed post-encephalitic parkinsonism improved mentally. He speculates, with an eye to the chlorpromazine-induced cases, that there may well be an "antagonism between the extrapyramidal hypokinetic syndrome and the schizophrenic process."

One is tempted to generalize this observation and state that the brake upon spontaneous psychomotor activity applied by these drugs may be of assistance to certain schizophrenics who are never too far removed from their struggle with fantasies of world-destruction. Drug parkinsonism may, as Sainz believes, represent merely a more pronounced degree of immobilization. Virtually all authors agree that even extreme instances of this complication are borne without complaint by patients although their physicians may feel misgivings. It is noteworthy that drug-parkinsonism has been observed in all degrees of severity. Because of varying diagnostic criteria, the reported incidence of "parkinsonism" varies greatly from institution to institution. Many *formes frustes* have doubtless been considered to exhibit merely "reduced psychomotor activity." If, as Cooper[4] states, the diagnosis of parkinsonism can be made from loss of associated movement of one arm, the high incidences reported by some (Brooks, 89%; Haase, 88%; Pleasure, 2/3 of cases) are readily understandable.

It does not seem unreasonable to suppose that the drug treated patients experience the reduction in psychomotility as a kind of armor against their troubles, as did our patient.[1] Leake[35] has suggested that a kinesthetic feed-back mechanism might operate here, a thought which had occurred to us in connection with the spontaneous armoring in our case.[1] Stengel[36] asked how the ego experiences the akinesia of paralysis agitans. Like Jelliffe,[37] he was struck by the similarity to catatonic catalepsy and recognized that ego function was not as impaired as in the latter condition. He explained the compulsive thoughts of parkinsonians as a manifestation of defused death-instinct, pointing out their frequent sado-masochistic content. This phenomenon was formerly thought by neurologists to indicate an organic basis for compulsion neuroses in general.

On the other hand, Buerger and Meyer-Gross[38] saw the ruminating compulsiveness of paralysis agitans as a result merely of damming up of blocked motoric impulses. Jelliffe[37] was impressed with the hostility bound up in the characteristic posture which he compared to that of a boxer. He[39] describes the case of a young man who, as the result of a post-encephalitic parkinsonism, found his hostile impulses uncontrollable and sought psychotherapy. At one point Jelliffe produced a "phasic mutation" (regression of the akinesia) by shaking the patient violently by the shoulders. The aggressivity liberated so threatened the patient that he disappeared from treatment for three weeks, later confessing that during the remission he would have been unable to control an impulse to kick the doctor. Here, the disease-enforced akinesia must originally have liberated a quantity of destrudo with which the patient then painfully learned to cope with Jelliffe's help. Temporary dissolution of the akinesia offered a tempting avenue of motor discharge for the very aggressions which it originally dammed-up and which were lately being dealt with by other means.

Stengel's[6] conception of an instinctual defusion in cases of paralysis agitans, which liberates a quantum of destructive drive, deserves most careful consideration. Perhaps, as he says, more is involved than mere reflux of dammed-up motoric impulses. He points as evidence to the "psychopathic" tendencies in children and adolescents which follow encephalitis in lieu of parkinsonism. Why, indeed, this difference? Stengel feels that there must be a disturbance of the superego which causes it to fail to cope with the liberated destructive impulses. Compul-

sive symptoms fail to develop in these juvenile cases. On the psychoanalytic level, one might postulate that the difference in superego development between child and adult might in some way be correlated with the difference in sequelae. The greater superego strength of the adult enables him to deal with the liberated destrudo by means of the parkinsonian characterologic-neurologic defense system. On a neurophysiologic level one could conceive that the disease, through some effect on the function of the centrencephalic system,* might diminish the individual's tolerance for anxiety and frustration. The analogy of an electrical condenser might be used here. In child and adult, brain disease might diminish the capacitance of this apparatus so that charges built up by the normal frustrations of life accumulate in amounts which it cannot handle. In the child this charge is almost immediately dissipated whereas the adult calls upon auxiliary apparatus to bind and store it.**

The concepts of MacLean[41] concerning the "visceral brain" and of Papez[42] regarding the neurologic mechanism of emotion enable us to visualize in neurologic terms how this auxiliary apparatus may possibly be brought into play. If, as Papez believes, the frontal lobes modulate the expression of emotion and impulse (superego function) via the uncinate fasciculus and its connections with the smell-brain and thence with the striatum, it is easily conceivable that the more mature frontal lobes of the adult may, by virtue of the greater traffic along this pathway, be able to contribute something (lacking in the child) which is necessary for the production of Parkinsonian akinesia. If this be true, we can understand why it is that symptomatology and neuropathology are so poorly correlated in this group of diseases, for a large functional element based upon psychic vicissitudes would presumably introduce an x-factor beyond the ken of neuropathologist or neurologist.

The characterologic predisposition described by Booth[43] (elaborating on the pioneer observations of Camp[44]) neatly fit into this concept. Germane to the present discussion is the alleged strong motor drive and tendency to aggressive action. These drives are, however, said to be channeled by their strong moralistic tendencies and social conformism, traits which among other things would distinguish them from the "acting out" patient who, willy-nilly, must seek an immediate escape from inner tension. It would appear that parkinsonian akinesia on any etiologic basis could, even in one and the same patient, have a double-edged effect: damming up of motoric drive (*a la* Buerger and Meyer-Gross) and armoring against eruption of aggressive impulses (*a la* Stengel and Jelliffe). Both of these aspects of the disease are consistent with Stengel's concept of instinctual defusion. The former would seem to aggravate the problem posed by the defusion whereas the latter would be a defense against destrudo derived from both the motoric damming effect and the instinctual defusion.

In applying the older knowledge of psychodynamics in paralysis agitans to the problem of drug-parkinsonism, one must keep in mind that the patients described by Booth,[43] Stengel,[36] Jelliffe,[37,39] and others were, for the most part, basically healthy personalities whose well-operating defenses were thrown off balance by an organic brain disease. On the other hand, the drug-parkinsonian patients are precisely those whose defenses are already severely impaired and who, as a result of drug therapy, are presumably moving in the direction of health. It is therefore necessary to effect a "transformation of coordinates" in attempting to predict the net result of the parkinsonian syndrome *vis a vis* the "metabolism" of aggressive drive.

Mindful of the apparent defensive usefulness of parkinsonian akinesia as a form of armoring, it seems not inconceivable that chlorpromazine and reserpine, through some complex neurochemical mechanisms, yet to be elucidated, might so alter the state of the centrencephalic system as to render more

*The hyperkinetic impulse disorders of children may be sequels of encephalitis or other insults to the central nervous system occurring at any time from the fetal period onward (usually during the first 5 years of life). One view, supported by recent experimental evidence from the work of Lauter Denhoff & Solomons (40), holds that the behavior disturbance is due to dysfunction of the diencephalon. In some cases no definite etiology can be ascertained.

**The favorable effect of chlorpromazine in these children (23) may be due to the inhibition of psychomotor outflow which permits time for the presumably undamaged but immature superego to exert its influence.

probable the development of such akinesia in service of ego-homeostasis. Certainly the spontaneous development of this phenomenon (Spiegel and Grinker,[2] Guggenheim and Cohen[1]) is rare (improbable) and appears to involve the most desperate disintegrative threat to the ego, under perhaps special and poorly understood conditions. If one wished to test experimentally the above hypothesis in regard to drug action, the problem would at once arise: upon precisely what bases should "proneness" to drug-parkinsonism be assumed to rest? It seems rather unlikely that the premorbid traits described by Booth[43] would apply here. The personality structure in question is powerful and efficient and possibly not to be found in a preschizophrenic population. Rather it would seem that "intra-morbid" factors might be crucial. From this point of view, one might suspect that the drug-parkinson patient would be one to whom the eruption of devastating hostility and destructiveness from within is an ever-present, consciously-felt threat opposed by a powerful superego. It might be possible, on this basis, to construct a rating scale for predicting the relative size and duration of dosage necessary to produce the disorder (in various degrees). The question of coincidental psychiatric improvement might then be studied in a more meaningful way. One would expect the most psychologically parkinson-prone patients to develop the disorder earlier, in severer form, on smaller dosages—and to show psychiatric improvement when they did so. In the present state of our knowledge, the smallness of dose necessary to produce parkinsonism appears to represent little more than an obvious measure of a *pharmacologic susceptibility.* Possibly a study along the lines just indicated would supply data to enrich the barren concept, *pharmacologic susceptibility.*

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BIBLIOGRAPHY

1. Guggenheim, P., and Cohen, L.: A Case of Schizophrenia in Which Manifestations of Parkinsonism Appeared During the Course of the Psychosis and Disappeared After Lobotomy. *Psychosomatic Medicine,* 20 (#2): 152-160 (Mar.-Apr.) 1958.
2. Grinker, R., and Spiegel, J.: War Neurosis in North Africa. The Tunisian Campaign (Jan.-May, 1943). *Josiah Macy, Jr. Foundation,* Sept. 1943, pp. 43-44.
3. Papez, J.: The Attitude Theory of the Emotions. Chap. VI, p. 92, Bull. Nine: *Nerv. & Ment. Dis. Monographs* (No. 81), New York, 1951.
4. Cooper, I.: The Neurosurgical Alleviation of Parkinsonism. *Chas. Thomas,* Springfield, Ill., 1956.
5. Mettler, F. A.: Relation Between Pyramidal and Extra-pyramidal Function. *Assn. Res. Nerv. Ment. Dis., Proc.,* 21: 150-227 (Chap. VI), 1942. Also: The Experimental Anatomico-physiologic Approach to the Study of Diseases of the Basal Ganglia. *J. Neuropath. & Exp. Neurol.,* 14: 115-141 (Apr.) 1955.
6. Kinross-Wright, V.: Remarks in "Chlorpromazine and Mental Health, Proceedings of Symposium Held Under Auspices of Smith, Kline & French Laboratories." *Lea & Febinger,* Phila., 1955, p. 59.
7. Moore, K. B.: Personal Communication, Ypsilanti State Hospital, Michigan.
8. Himwich, H., and Rinaldi, F.: Drugs Affecting Psychotic Behavior and the Function of the Mesencephalic Activation System. *Dis. Nerv. Syst.,* 16: 133 (May) 1955. See also Himwich, H.: Prospects in Psychopharmacology, *ibid.,* 17: 109 (Apr.) 1956.
9. Moruzzi, G., and Magoun, H. W.: Brain Stem Reticular Formation and Activation of the EEG. *EEG & Clin. Neurophysiol.,* 1: 455-473, 1949.
10. Jasper, H. H.: Diffuse Projection System: The Integrative Action of the Thalamic Reticular System. *EEG & Clin. Neurophysiol.,* 1: 405-419, 1949.
11. Bucy, P. C.: The Neural Mechanisms of Athetosis and Tremor. *J. Neuropath. & Exp. Neurol.,* 1: 224-239, 1942.
12. Magoun, H. W.: Chap. Anatomy in "Parkinsonism and Its Treatment," Ed. L. J. Doshay. *Lippincott,* Phila., 1954.
13. Rhines, R., and Magoun, H. W.: Brain Stem Facilitation of Cortical Motor Response. *J. Neurophysiol.,* 9: 219, 1946.
14. Mettler, Ades, Lipman and Culler: The Extrapyramidal System: An Experimental Demonstration of Function. *Arch. Neurol. & Psychiat.,* 41: 984-995, 1939.
15. Murphy and Gellhorn: *J. Neurophysiol.,* 8: 431-447, 1945.
16. Ingram, Barris and Ransom: *Arch. Neurol. & Psychiat.,* 35: 1175, 1936.
17. Magoun, H. W.: Caudal and Cephalic Influences of the Brain Stem Reticular Formation. *Physiol. Rev.,* 30: 459, 1950.
18. Spiegel, E. A., Wycis, H. T., Baird, H. W., Roomer, D., and Thur, C.: Pallidum and Muscle Tone. *Neurol.,* 6: 350 (May) 1956.
19. Davison, C.: The Role of the Globus Pallidus and Substantia Nigra in the Production of Ri-

gidity and Tremor. *Proc. Assoc. Res. Nerv. Ment. Dis.,* 21: 267-333 (Chapt. IX).

20. Azima, H., and Richman, A.: Alteration of Copper Metabolism in Chlorpromazine Treated Cases. *Arch. Neurol. & Psychiat.,* 75: 163-166 (Feb.) 1955.
21. Lehmann, H. E.: Symposium on Chlorpromazine, Part II. *J. Clin. & Exper. Psychopathol. and Quart. Rev. of Psychiat. & Neurol.,* 17: 129 (Apr.-June) 1956.
    b. Lehman, H. E., and Hanrahan, G. E.: Chlorpromazine, a New Inhibiting Agent for Psychomotor Excitement and Manic States. *Arch. Neurol. & Psychiat.,* 71, 225 (Feb.) 1954.
    c. Lehman, H. E.: Selective Inhibition of Affective Drives by Pharmacologic Means. *Am. J. Psychiat.,* 110: 856 (May) 1954.
22. Sarwer-Foner, G. J., and Ogle, W.: Psychosis and Enhanced Anxiety Produced by Reserpine and Chlorpromazine. *Canad. Med. Assn. Jr.,* 74: 526 (Apr.) 1956.
23. Schmiedeck, R.: An Attempt to Explain Thorazine Failure in Terms of Personality Structure. Thesis submitted to the Meninger School of Psychiatry, 1955.
24. Freed, H.: a) Use of Chlorpromazine in Child Psychiatry in Symposium on Chlorpromazine, Part II. *J. Clin. & Exp. Psychopathol. & Quart. Rev. Psychiat. & Neurol.,* 17: Apr.-June, 1956.
    b) Remarks in Chlorpromazine and Mental Health, Proceedings of Symposium Held Under the Auspices of Smith, Kline & French Laboratories. *Lea & Febiger,* Phila., 1955, pp. 112-117.
25. Sainz, A.: Chlorpromazine and Mental Health, Proc. of the Symposium held under the auspices of Smith, Kline & French Laboratories. *Lea & Febinger,* Phila., 1955, p. 72-3.
26. Pleasure, H.: *Ibid.* (SKF Symposium, 1955) p. 55.
27. Ayd, J., Jr.: a) *Ibid.* (SKF Symposium) p. 56.
    b. Large Doses of Chlorpromazine in Treatment of Psychiatric Patients. *Dis. Nerv. Syst.,* 16 (#5): 146 (May) 1955.
    c. Remarks in Psychiatric Research Report #4. An Evaluation of the Newer Psychopharmacologic Agents and Their Role in Current Psychiatric Practice." *Am. Psychiat. Assn. (Galesburg Conference),* Washington, 1956, p. 66.
    d. Physiol. and Neurol. Actions of Chlorpromazine. *APA Psychiat. Res. Reports,* 1: 14-24.
28. Brooks, G.: a. SKF Symposium, p. 51.
    b. Experience with the Use of Chlorpromazine and Reserpine in Psychiatry with Especial Reference to the Signicance and Management of Extrapyramidal Dysfunction. *New Eng. J. Med.,* 254: 1110-1123, June 14, 1956.
29. Haase, H. J.: a. Über Vorkommen und Deutung des Psychomotorischen Parkinson-syndrome bei Megaphen bzw. Largactil Dauerbehandlung. *Nervenartz,* 25: 486-492, 1954.
    b. Psychiatrische Erfahrungen mit Megaphen (Largactil) und dem Rauwolfia Alkaloid Serpasil unter der Gesichtpunkt des Psychomotorischen Parkinson syndroms. *Nervenartz,* 26: 507-510, 1955.
30. Kinross-Wright, V.: a. *Postgrad. Med.,* 15: 297, Oct. 1954.
    b. Complications of Chlorpromazine Treatment. *Dis. of Nerv. Syst.,* 16 (#4): 114-119 (Apr.) 1955.
31. Goldman, D.: a. Remarks, Galesburg Symposium, p. 86.
    b. SKF Symposium, The Effects of Chlorpromazine on Severe Mental and Emotional Disturbances. Pp. 19-40.
32. Kline, N.: Clinical Applications of Reserpine. Psychopharmacology. Symposium. Publ. No. 42 of AAAS, Wash., D.C., 1956, p. 93.
33. Doshay, L. J.: *J.A.M.A.,* 156: 680-684 (Oct. 16), 1954.
34. Staehelin, J. E.: Einige allegemeine Bemerkungen über die Largactiltherapie in der Psychiatrischen Universitätsklinik Basel. *Schweitz Arch-f. Neurol. u. Psychiat.,* 73: 228-291, 1954.
35. Leake, C.: Remarks in a Forum delivered at Winter Veterans Hospital, Topeka, Kansas, Nov. 7, 1956.
36. Stengel, E.: Zur Kentniss der Triebstörungen und Abwehrreaktionen des Ichs bei Hirnkranken. *Int. Z. f. Psa.,* 21: 544-560, 1935.
37. Jelliffe, S. E.: The Mental Picture in Schizophrenia and in Epidemic Encephalitis. *Am. J. Psychiat.,* 6: 27, 1927.
38. Buerger and Meyer-Gross: Über Zwangssymptome bei Encephalitis Lethargica und über die Strukture der Zwangserscheinung Überhaupt. *Zentralblat, f. Nervenh. u. Psychiat.,* 115: 1928.
39. Jelliffe, S. E.: The Parkinsonian Body Posture. *Psychoanal. Rev.,* 27: 467, 1940.
40. Laufer, M. W., Denkott, E., and Solomons, G.: Hyperkinetic Impulse Disorders in Children's Behavior Problems. *Psychosom. Med.,* 19: 38-49 (Jan.-Feb.), 1957.
41. MacLean, P.: Psychosomatic Disease and the Visceral Brain. *Psychosom. Med.,* 11: 338-353, 1949.
42. Papez, J.: A Proposed Mechanism of Emotion. *Arch. Neurol. & Psychiat.,* 38: 725-743, 1937.
43. Booth, Gotthard: Psychodynamics in Parkinsonism. *Psychosom. Med.,* 10: 1-14, 1948.
44. Camp, C. D.: Paralysis Agitans in "Modern Treatment of Nervous and Mental Diseases," Ed. White & Jelliffe, Phila,, 1913.

Treatment in Private Practice

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An inspiration in the realm of follow-up was Dr. Walter Freeman's presentation at the meeting of the Southern Medical Association in Miami Beach last fall, in which he related his 10 to 20 year study of 500 cases of prefrontal lobotomy. He explained that, in response to a challenge by Dr. Adolph Meyer he had made a close personal follow-up of one hundred per cent of these patients. Prompted at least in part by Dr. Freeman's report is this effort to review the status of patients seen in a decade of private practice in psychiatry.

At the May meeting of the Florida Psychiatric Association, Dr. William M. C. Wilhoit reviewed three months of his private practice of psychiatry in Pensacola. His paper gave an excellent picture of the practice of general psychiatry with an eclectic approach.

Jacksonville, located in the northeast corner of Florida, is a city of stable economy with a population that has grown from 206,442 in 1946 to 226,100 in 1956, while the population for Duval County has grown from 273,843 to 398,000 in this decade. The community draws patients from a wide area of northeast Florida and southeast Georgia. The number of psychiatrists in private practice in the community increased from three in 1946 to seven in 1956.

Throughout the decade the pressure for psychiatric care was very great. Several general hospitals, including a private colored hospital, were available for mild psychiatric disorders in patients requiring hospital treatment. Two nursing homes in the community were prepared to handle disturbed patients as well as milder ones. In 1949 the Duval County Hospital (now the Duval Medical Center) opened a forty-bed psychiatric building with locked wards. Primarily for the care of indigent patients, this facility was available to pay and part-pay patients who have constituted approximately one third of the admissions there. This facility has been available for outpatient electrotherapy and carbon dioxide therapy. Outpatient insulin therapy, in addition to outpatient electro-therapy and carbon dioxide therapy is provided by the nursing homes. Service patients, cared for on a volunteer basis, have formed a sizable case load but are not included in this series.

In the early records of this series many house calls are noted. A house call now is a rarity. Office consultations made up at least half of the working day. As the number of hospital admissions rose, the percentage of time available for office visits decreased and since 1952, with rare exceptions, only patients requiring hospital care have been accepted as new patients, available office time being saved for old patients and follow-up of hospital patients. Fortunately, several more recent additions to the local group of psychiatrists have preferred office psychiatry, so patients requiring only office therapy are well cared for.

In the series of patients presented, psychotherapy was carried out in the conversational method with a good deal of interpretation and no non-directive therapy. Scarcely any patient, even if seen only once in diagnostic consultation, got by without some psychotherapy. In analyzing methods of treatment, however, those listed as having been treated by psychotherapy are those in whom this has been a major form of treatment. In all patients with whom some conversation was possible, an effort was made to help the patient attain some degree of understanding of his illness and its origins and a greater understanding of himself. Physical treatments included classical electroshock, electro-stimulation, insulin subshock, insulin coma, and carbon dioxide. Various medications were used, with the general principal of reducing medication to a minimum as quickly as possible.

In this study an attempt has been made to review the office and hospital records of all private patients seen between January 1946 and January 1956, recording on individual punch cards each patient's name, address, age, sex, color marital status date of first visit, total number of office visits and period of time covered, number of hospital

admissions and total hospital days, the diagnosis, treatment, condition on termination, and disposition.

Approximately 2150 letters were sent out. There have been 461 replies. There has been insufficient time for other steps toward obtaining follow-up information or trace the present address for the many patients whose letters were returned because the patient had moved.

Diagnostically, the number of patients in each category was as follows: psychoneurotic reaction 763, alcoholism (including acute and chronic brain syndromes) 451, affective reactions 212, schizophrenic reactions 157, personality disorders 154, transient situational personality disorders 151, chronic brain disorders 104, paranoid states 57, no psychiatric disorder or no diagnosis made 39, acute brain disorders (exclusive of alcohol) 22, psychophysiologic autonomic and visceral disorders 20, mental deficiency 17, psychotic reaction, unclassified 1. There were 82 cases of neurological disorders of which 49 were convulsive disorders.

Of the total number of patients seen, almost half were from Jacksonville and its environs, 35% from Florida and Georgia, and about 15% from other areas. The total number of white males was 1022, of white females 1018—almost the same. Only 15 colored patients are included, as tabulations at the colored hospital have not been completed. The totals according to age were broken down into decades; 64 were under 10, 163 between 10 and 20. There were 360 who were in their twenties, 383 in their thirties, 454 in their forties, 184 in their fifties, 103 in their sixties, 33 in their seventies, and 14 in their eighties. There were 1164 patients on office visit; 1231 were hospitalized or seen as hospital consultations. In all, 336 patients were seen in consultation or for evaluation only either at the office or in a hospital. In 590 patients, psychotherapy was a major part of the treatment, 627 were treated with insulin sub-shock, 42 with insulin coma, 549 with drugs, 67 with carbon dioxide, 428 with electroshock.

There were 54 classed as recovered, 1451 improved, 668 unimproved, 11 died. Of the total series 52 patients were transferred to a VA hospital or a private hospital elsewhere. No patient died as the result of insulin or electroshock. Three patients committed suicide while under treatment; 11 patients were reported to have committed suicide later. Since treatment 78 were reported to have died. Of the patients who have returned the questionnaire, 120 report themselves most helped by psychotherapy, 65 by medicine, 51 by insulin, 70 by electric treatments, five by carbon dioxide, and 33 by general hospital care.

Electro-therapy may some day be replaced by other methods, but it has served us well and is still of great value in depression and early schizophrenia. One of the suicides was a patient for whom electroshock was considered too great a risk because of a history of earlier coronary occlusion. Since then a few patients with known cardiac disease but with serious mental disorder have received electroshock without apparent damage. One woman in her 60's with known cardio-renal disease, diabetes, and a history of bowel resection for carcinoma was in an agitated depression of such severity that electroshock was considered worthy of the added risk. She made a complete recovery from her depression and enjoyed six months of useful business and social life before dying suddenly one night at home. Another patient with a menopausal schizo-affective reaction began electroshock in 1951. Each time treatments were stopped she rapidly developed paranoid and depressive symptoms and treatment was resumed. Tranquillizers have helped only in that they may have played a part in lengthening the period between treatments to two weeks. She has now received 496 treatments. She has little apprehension about the treatments, which she takes as an out-patient, meantime keeping house, enjoying her church, the dog tracks, and other social activities, often accompanying her husband on business trips. There is no evidence of any deterioration.

A total of 451 patients, with the men outnumbering the women 2 to 1, were classed in categories related to alcoholism. Of these, 44 were classed as having acute brain syndrome. Almost all were treated as hospital patients or as hospital patients with office follow-up. In addition to the usual vitamins and the sedatives or tranquilizers used in

withdrawal from alcohol, 182 were treated with insulin sub-shock; 95 per cent were hopefully classed as improved.

Of the patients with alcoholism, follow-up has been obtained on 63. Of those who responded, three did not recall having been in the hospital under my care, 15 considered themselves cured, 13 improved, 34 reported themselves as unimproved or worse, 26 were reported to have died, 15 considered themselves helped most by medicine or hospital care, 10 by insulin, 21 by our talks.

Of the total 763 patients, 47 per cent were classed in the category of psychoneurotic reaction. Here the women outnumbered the men 2 to 1; 333, or 44 per cent of this total group, were treated with psychotherapy as a major part of their treatment; 258, about one third, received insulin subshock; 190 were treated with drugs; 117 received electroshock and 52 received CO_2. Most were given a combination of treatments. There were 389 patients, about 75 per cent, classed as improved, 214 as unimproved or worse, one died of unrelated cause; 135 reported themselves recovered or improved, seven as unimproved; 16 were reported to have died since they were seen and three to have died by suicide. A total of 89 considered themselves helped by talks, 23 by medicine, 28 by insulin, 22 by electroshock, eight by general care. One patient with mild chronic psychoneurosis, who still comes in for office visits, was first seen at home in 1940 at the age of 75 in an acute brain syndrome which responded to hydration and vitamins, with nursing care at home. At 93 she does most of her own housework but is still "nervous."

In this survey 157 were classed as schizophrenic reaction of whom 99 were treated with electroshock, 31 with insulin coma, 36 with drugs; 66 received insulin sub-shock, usually on alternate days with electroshock. In 22 cases, psychotherapy was a major part of treatment. Seven cases were considered recovered, 99 improved; 21 were transferred to a state hospital or a VA hospital and 11 are still current. Eight reported themselves as recovered, 17 as improved, seven as unimproved or worse. Three were reported to have died. One patient, after later treatment in another hospital, was reported to have killed her husband, her son, and herself.

Classed as psychotic affective reactions were 212 cases. Of these, 14 were seen only in diagnostic consultation, 161 were treated with electroshock, 84 with drugs, 46 received insulin sub-shock, and 30 received a notable amount of psychotherapy. Fourteen were listed recovered, 166 as improved, 29 as unimproved. One patient died of unrelated causes and one of suicide. Nine patients were transferred to the state hospital and six to other hospitals. Of those replying to the follow-up letter, 18 reported themselves well, 24 improved, seven unimproved. Eleven patients had died, three by suicide. Ten patients thought medicine helpful, 26 electroshock, and 12 the talks.

The 151 classed in the category of transient situational personality disturbances were, for the most part, seen briefly, 110 for consultation only. Only 18 had more than five office visits and only 18 were hospitalized; 89 of this category were children or adolescents. Follow-up was obtained on 24; 11 were reported as recovered, six as improved, four as unimproved. Seven had died and one was reported to have committed suicide. Several appreciative letters in this group pointed up the potential value of a brief psychiatric contact in time of stress.

Of the 104 cases of chronic brain disorders, 18 were associated with convulsive disorder; 43, or half the remaining cases, as would be anticipated, fell into the older age group. Twenty-two were seen in consultation only. The remainder were treated chiefly with drugs, though five also received insulin subshock and seven electroshock. Of the total group, 42 were classed as recovered or improved, 55 as unimproved, one died, and one is current. Of the 25 follow-ups in this group, one considers herself recovered, five are improved, three unimproved, and 11 have died.

The 22 cases of acute brain disorder, exclusive of alcohol, are evenly distributed in age groups. One was not treated, 20 were treated with drugs, eight also received insulin sub-shock and one psychotherapy. Sixteen were improved, two unimproved, and three died. Six follow-ups were obtained of whom two are recovered, one improved and three died.

Of the 20 cases classed as psychophysiologic autonomic and visceral disorders, seven were not treated, eight were treated with psychotherapy, five with insulin sub-shock, two with carbon dioxide therapy, three with electrotherapy, three with drugs. Three patients with intractable pruritis vulvae responded dramatically to carbon dioxide; 11 of the 13 treated were closed as improved. Of six on whom we have follow-up, two have since died, one is worse, one improved and two recovered. One each attributes improvement to electrotherapy, drugs, and psychotherapy.

In 57 cases classed as paranoid state, 10 were seen for evaluation or consultation only, 16 received psychotherapy, 33 were treated with insulin, 16 with drugs. Two were closed as recovered, 34 improved, 19 unimproved. Two patients report themselves well, three improved, one unimproved. Four credited psychotherapy for their improvement, one medication, two insulin treatment, and one electrotherapy.

The follow-up questionnaire has brought in many interesting replies. In addition to those expressing appreciation there have been others. "I only saw you once. You kept me waiting two hours and that was too much!" "I saw you only one time. I was cured by Dr. Moore." One simply placed an exclamation point after "Fine" and added "I got a divorce." One of the most gratifying was the letter from a mother who, with the father, had once brought in her mildly retarded boy for consultation and advice. They were seen one time. She describes his happy adjustment through a special class, two years in the army and now as a self-supporting delivery boy for a dental firm. She writes, "I think Bert has developed as well as we might hope and I think the essential thing was that we ourselves needed to understand Bert and the nature of his problem."

Discussion

The follow-up in this series falls far short of Dr. Freeman's 100 per cent with constant contact with each patient or family. It is planned to make this a continuing study with hopes for improvement in methods of recording as well as in follow-up.

The series of cases reviewed is considered typical of the practice of the psychiatrist in private practice. Some practices would evidence a greater emphasis on office psychotherapy, others a greater emphasis on court work, others a higher percentage of neurological cases. All, however, are beset by the tremendous need and demand for psychiatric help within the community.

This points up again the need to train more psychiatrists and the need for research in treatment and prevention of psychiatric disorders. It behooves each of us to stimulate recruitment for training and, if possible, to participate in training programs. It would be helpful, not only to an individual's evaluation of his work, but to the field of research in the epidemiology of psychiatric disorders if all of us in private practice could agree on a recording system similar to the punch cards used for this study, thus making our work available for larger statistical studies that might eventually lead to improvement in treatment and prevention of mental disease and to the promotion of good mental health in our communities.

Patient Improvement and Psychiatric Nursing Care

GORDON R. FORRER, M.D., and JAMES L. GRISELL, PH.D.

Psychiatric nurses are employed in a large number of mental hospitals, public and private. These people are employed on the assumption that they make a direct contribution to the recovery of patients. A corollary may be that an increase in nursing care through increased staff will be reflected in an increase in the number of patients discharged. However, this assumption has not been empirically demonstrated. The purpose of this research was to determine if the addition of nurses to wards would result in an increase in the number of patients released from such wards as compared with control wards.

Methods

The basic method employed in this study was a comparison of objective measures of nursing activity on experimental and control wards. The nul hypothesis tested was that the addition of psychiatric nurses produced no difference between the experimental and control wards on the measures studied. Four wards, two experimental and two control, were used in this study. They were located on the male side of the Intensive Treatment Building at the Northville State Hospital. Two wards were on the first floor and the other two were on the second floor, directly above. The first floor wards were closed wards and were used for intensive treatment of acutely ill psychiatric patients. The second floor wards were open wards and were used for continuing treatment of convalescent psychiatric patients. One first floor ward and the second floor ward directly above it, were designated as experimental wards, the other two wards were used as a control. Each ward had a capacity of 32 patients.

The control wards were each staffed with a single psychiatric nurse on the day shift only, Monday through Friday. On the open, upstairs ward there was a psychiatric aide on each shift. On the closed, downstairs ward there were three psychiatric aides on each shift.

From Northville State Hospital, Michigan.

The experimental wards were staffed with two psychiatric nurses on the day shift and one psychiatric nurse on the afternoon shift. These nurses did not work on Saturday or Sunday. These wards had the same number of psychiatric aides as the control wards.

The training and experience qualifications of the nurses on each of the wards is presented in Table 1.

The four wards in the study were under the care of two physicians, one serving the two open, upstairs wards and the other serving the two closed, downstairs wards. Thus the physicians variable was confounded with the open-closed ward variable.

When the study was initiated, the wards comprised patients in various phases of treatment. In order to be sure that each ward did not differ from its counterpart, as far as patients were concerned, the patients in the area were reassigned at the beginning of the study. However, this reassignment was done horizontally. The patients in the two upstairs wards were pooled. Then, those who had even case numbers were assigned to the experimental ward, and patients with odd case numbers were assigned to the control ward. A similar procedure was followed for the downstairs closed wards.

Control was exercised over the transfer of patients into, within, and out of the study wards. When a transfer was to be into the area, the physician would designate to which floor the patient was to be sent. Whether the patient was well enough to reside on an open ward, or on a closed ward was a medical decision. However, once the physician had designated the floor, the actual ward experimental or control, was an experimental decision made by random selection. The physician in charge of the male service, who made all ward assignments, was provided with a list of random numbers. A transfer with even number was sent to the experimental ward. If it was odd, he was sent to the control ward. If the ward suggested by the random numbers was full, then he was sent to the other ward.

Once a patient was in the study area, he

TABLE 1

Training and Experience of Each Nurse Participating in the Study

Nurse, ward worked, and time in study	*Education*	*Experience*
OPEN EXPERIMENTAL		
1. 3/6/56 - 9/6/56	B.S. in nursing, Wayne State U.	No experience until employed in research project.
2. 3/6/56 - 6/9/56	Ford Hospital, Detroit.	2½ years psychiatric nursing at NSH before study began.
3. 6/11/56 - 8/17/56	Mt. Carmel Hospital, Detroit, and 1 year at St. Louis U.	1 year psychiatric nursing experience at NSH before study began.
4. 3/6/56 - 9/6/56	Bellevue Hospital, N. Y. C., B.A. in nursing, Wayne State U.	2 years Public Health Nursing in N. Y. C. and 1 year as general staff nurse in Detroit.
CLOSED EXPERIMENTAL		
5. 3/6/56 - 8/17/56	B.S. in nursing, Wayne State U.	1 year non-psychiatric nursing prior to study.
6. 3/6/56 - 8/10/56	B.S. in nursing, Wayne State U.	No experience until employed at NSH in this project.
7. 3/6/56 - 9/6/56	B.S. in psychiatric nursing, Mercy College, Detroit.	1 year general nursing before being employed for nursing study.
8. 8/20/56 - 9/6/56	Same nurse as 3 above.	Same nurse as 3 above.
OPEN CONTROL		
9. 1/6/56 - 9/6/56	Grace Hospital, Detroit.	1 year at NSH before study began.
CLOSED CONTROL		
10. 3/6/56 - 9/6/56	Ford Hospital, Detroit.	2 years at NSH before study began.

could be transferred only vertically within the area. A patient on the experimental side stayed there. If he was transferred into the closed ward, then sent to an open ward after improving, it had to be to the ward above, the open experimental ward, if he remained in the study area. The same was true for the control wards. If a patient was to be transferred out of the study area, there was no restriction on such a move. However, if a patient was transferred back to the study area, he again went to the same side where he originally resided.

When the study was begun every effort was made to keep the study wards as "natural" as was possible. All four wards functioned as regular hospital wards, with no special concessions or privileges granted. The only difference was the presence of the extra nurses on the two experimental wards.

The only departure from this ideal situation, which was purposefully contrived, involved the recording of activities by the nurses. No other nurses in the hospital kept such detailed records of their activities as did the nurses in the study area.

Sources of Data for the Study

Whether the addition of nurses to a ward will have any effect on the patients is a complex study. It was felt that the presence of the extra nurse should make itself felt in many indirect ways other than the discharge rates from the wards. These indirect manifestations of the extra nurse were felt to be important in gaining insight into the ways in which nurses affected the movement of patients. Accordingly, detailed records were compiled of many different variables.

There were four primary sources of information about the activities taking place on a ward: (1) the doctor's daily log; (2) the nurse's daily log; (3) the daily hospital census; and (4) miscellaneous forms used in the hospital.

The doctor's daily log is filled out by the ward personnel containing requests or items about patients which must be brought to the doctor's attention. These were then classified according to a system worked out for this study. The following items were obtained from the doctor's daily log.

1. Psychiatric management.
2. Patient contacts (talks with patients of less than 5 minutes duration).
3. Patient interviews (talks with patients of more than 5 minutes duration).
4. Tranquilizing agents (request for a renewal order).
5. Medication (medical, request for a renewal order).
6. Medications (stat sedation).
7. Physical diagnosis and treatment.
8. Requests for laboratory work-up.
9. Visitor requests.
10. Requests for patients to phone outside hospital.
11. Social Service.
12. Somatic therapy.
13. Occupational therapy request.
14. Work therapy requests.
15. Outside work requests.
16. Family care requests.
17. Privilege card requests.
18. Leave of absence requests.
19. Miscellaneous.

The nurse's daily log was filled out by each nurse in the study. On this she recorded her activities and, if an activity was carried out with five or fewer patients, she listed the patients, otherwise she merely indicated the number of patients involved.

The activities on the nurse's daily log were classified according to the following:

1. Doctor directed nursing care:
   a) Nourishments.
   b) Ward cleaning..
2. Nurse initiated activities.
3. Therapy A activities (routine, group activities):
   a) Gym.
   b) Snack bar.
   c) Ward meetings.
   d) Movies.
   e) Walks.
   f) Dances.
   g) Parties.
   h) Television.
   i) Library.
4. Therapy B activities (by prescription):
   a) Occupational Therapy.
   b) Work Therapy.
   c) Recreational Therapy.
   d) Bowling.
5. Stat Sedation.
6. Seclusions and unusual incidents.
7. Transporting patients (to and from clinics, conferences, etc.).
8. Attendant initiated activities.
9. Patient initiated activities.

The following kinds of items were picked up from the hospital's daily census.

1. The granting or revocation of the hospital's three kinds of privilege cards:
   a) Ground.
   b) Building.
   c) Transportation (to and from work area only).
2. Leave of Absences.
3. Transfers within the study area.
4. Transfers into or from the study.

From various forms and permission slips used in the hospital the following additional information was obtained:

1. Rides with relatives.
2. Visitors slips.
3. Reports of unusual incidents (injuries, etc.).
4. Seclusions.
5. O. T. prescription forms.
6. Work Therapy prescription forms.
7. EST treatments.

This information was collected daily and tabulated in two ways, by patient and by ward. A record was kept of the frequency with which all these things happened in regard to each patient, and the frequency with which they occurred on each of the four study wards.

There was one other source of data obtained in this study. This was the work sampling procedure used for all nurses in the area. This was done in an effort to show that the psychiatric nurses were all doing the same things with their patients. Any differences between the experimental and control wards could then be attributed to an increase in nurses, giving the same kind of care, rather than differences in the things done by the nurses. Our hypothesis in this study deals only with the number of nurses and it assumes they are engaging in the same kinds of activities. Whether they did was a matter to be empirically determined.

This determination was made by the utilization of the same work sampling technique utilized in the work sampling study done at Northville State Hospital and reported in the June 1956 issue of *Nursing Research*. The only difference between the Northville study and our study was the number of observations made on each person. For this study there were 40 observations made on each nurse over a three month period. An observation was made during each of the 40 hours of their normal work week.

Results

Our results were derived from an analysis of the four different kinds of data collected

during the course of the study: the frequency with which different kinds of data were recorded on the doctor's log, the nurse's log, the daily census, and the observations of the nurse's job performance.

To better analyse the material on the doctor's log, the nurse's log and the daily census which was pertinent to this study, a daily record was kept of the frequency with which all the classified items occurred on each of the four study wards and weekly sums were computed. These were then subjected to an analysis of variance type treatment. The particular analysis which was employed yielded three kinds of comparison: (1) a comparison of the mean weekly frequency of each category for the experimental and control wards; (2) a comparison of mean weekly frequency for the open and closed wards, and (3) the interaction effects of these two main effects.

The data of this study was somewhat cumbersome to analyse because the variance in the comparisons was not homogeneous. Consequently, it was necessary to employ transformations to equate variances before running the analysis. For the most part, square or cube root transformations were utilized. Transformations make the interaction effects additionally difficult to interpret. There-

TABLE 2

Results of Activities Recorded on Doctor's Log

Category	Transformation	Exper. Mean	Control Mean	Mean Diff.	F	Open Mean	Closed Mean	Mean Diff.	F
Psychiatric Management	cube root	1.17	1.33	.16	—	.94	1.57	.63	27.8 P<.001
Patient Contacts	——	5.00	4.81	.19	—	4.98	4.83	.15	—
Requests for Tranquilizing Drugs	cube root	4.98	8.96	3.98	6.62 P<.05>.01	5.33	6.67	1.43	4.87 P<.05>.01
Medications	——	3.43	4.12	.69	—	2.98	4.57	1.59	8.25 P<.01
Work Therapy Requests	cube root	1.76	1.76	—	—	.33	3.19	2.86	77.72 P<.001
Privilege Card Requests	cube root	1.28	.22	1.06	8.77 P<.01	.33	3.12	2.79	65.89 P<.001

TABLE 3

Results from Nurse's Log

Category	Transformation	Exper. Mean	Control Mean	Mean Diff.	F	Open Mean	Closed Mean	Mean Diff.	F
Doctor directed nursing care—number of patients	cube root	81.48	10.52	50.96	158.91 P<.001	50.96	41.04	9.92	5.21 P<.05>.01
Nurse initiated activities	cube root	79.24	14.90	64.34	57.23 P<.001	50.72	43.43	7.29	—
Nurse initiated activities—number of patients	cube root	234.56	36.15	198.41	186.47 P<.001	140.69	128.00	12.69	—
Therapy A activities	square root	100.19	39.44	60.75	50.8 P<.001	72.78	66.85	5.93	—
Therapy A activities—number of patients	square root	99.93	50.94	48.99	52.8 P<.001	75.35	75.52	.17	—
Patient initiated activities	square root	47.72	9.28	38.44	220 P<.001	29.65	27.35	2.30	—
Patient initiated activities—number of patients	cube root	124.93	18.56	106.37	222.9 P<.001	73.46	70.02	3.44	6.28 P<.05>.01

fore, none of them will be considered in arriving at our results.

The results for material contained in the doctor's log is given in Table 2. This table shows the categories in which significant differences were found. The two most interesting findings from our point of view are those involving the experimental and control wards. The number of requests for tranquilizing drugs was smaller on the experimental wards. Also, the number of requests for privilege cards was greater for the experimental and less for the control wards. These results would suggest that the experimental wards, with their additional help, were more successful in handling patients with psychiatric nursing techniques, hence, fewer chemical controls were needed.

The significant F's involving the open-closed comparison are in categories where, because of the nature of open and closed wards, these results would be expected. There is more psychiatric management required for the closed ward patients as they are more acutely ill. The larger number of requests for tranquilizing drugs on the closed ward may reflect the same kind of phenomena. The greater number of medication requests may be explained by the fact that the patients are on the ward more on the closed wards than on open wards. Thus, conditions which require medication may be brought to the nurse's or doctor's attention more readily than on open wards. The small number of work therapy requests from the open ward is a function of the fact that one requirement of patients before being sent to an open ward is that they have a hospital work assignment. These results, pertaining to open-closed comparisons, must be viewed as tentative because this variable is confounded with the physicians variable.

Table 3 gives the significant findings for the categories of items taken from the nurse's log. In this table the largest number of significant findings is found in the comparison between the experimental and control wards. Actually, for every item, there was a significant F for this comparison. These items all have to do with the activities of nurses with patients. These results reflect very clearly the effects of extra help on the wards. There are more contacts with more patients on the experimental than on the control.

Also of interest, but more difficult to explain, are the two significant F's found for the open-closed comparisons. One would not have predicted in advance that there would have been more patients involved in doctor directed nursing on the open, rather than the closed, wards. This may well be due to the fact that different doctors worked on the wards involved and this finding may be reflecting doctor differences as much as ward differences.

The second significant finding in the open-closed comparison involves the number of patient initiated activities which were greater on the open than on the closed wards. This is probably a function of the improved status of the patient but it could also reflect doctor differences as well.

A second source of information obtained from the nurse's log was the listing of individual or small group contacts between nurses and patients. For each ward, the number of nurse initiated and the number of patient initiated contacts were tabulated for each patient. To compensate for the fact that the patients were sometimes on leave and thus not available for nurse-patient contacts, the ratio of nurse-patient contacts to days in residence on the ward was computed for each patient. The patients on each ward were then divided up into three groups. Group 1 was composed of all patients who had a positive transfer from the ward. A positive transfer being defined as any transfer to a more comfortable ward, to a family care placement, to convalescent status or to discharge. Group 2 consisted of the patients who remained in the study area from the time they were sent there until six weeks after the termination of the study. This six week period was arbitrarily chosen. Group 3 consisted of those patients who had a negative transfer from the study area. A negative transfer being defined as a transfer to any psychiatric ward that was not more comfortable.

For each ward in the study the three groups were compared on their ratio of nurse initiated contacts to days in residence, and on their ratios of patient initiated contacts

in Table 4. The analyses for the patient-initiated contacts yielded no significant findings. However, for the nurse initiated contacts, for the experimental wards, the ratios of nurse initiated activities to days in residence were significantly smaller for the group with positive transfers than for the other two groups. There was no difference for the control wards on this variable. This indicates that the nurses tended to have fewer contacts with the patients who got better and left the ward than she did with the ones who remained on the ward or had a negative transfer.

TABLE 4

Mean Number of Nurse Initiated Activities Per Patient for the Three Groups of Patients

	Group 1	2	3	F
Open Experimental	.76	1.09	.94	4.9 P<.05>.01
Closed Experimental	.40	.96	.67	7.07 P<.05>.01
Open Control	.07	.09	.07	NS
Closed Control	.20	.16	.16	NS

The significant categories for information derived from other forms are found in Table 5. Here we see that all significant differences are found in open-closed ward comparisons while there are no differences between the experimental and control wards. In each instance, all the significant differences favor the closed wards. Of greater interest here is the fact that there were no differences in the experimental and control wards in regard to the number of patients who had a positive transfer. Although, as seen in all the results up to this point, there were differences between the experimental and control wards, there was not a greater number of discharges or positive transfers from the experimental as compared to the control wards, as our hypothesis suggested there would be.

The last source of data obtained from this study was a comparison of the activities of the nurses as revealed by spot observations during the course of the study. These results are given in Table 6.

This table shows that all the nurses are engaged in the same kind of duties except the two nurses on the closed experimental ward. These two were observed more frequently engaging in doctor directed psychotherapeutic activities.

Discussion

Although the results of our study do not support the hypothesis advanced in this investigation there are some reasons why this might have happened. In the first place, the study lasted only six months. This is not a very long time to observe the effects of a variable on mentally ill patients where hospitalizations frequently last for more than a year. Had the study been prolonged a difference might have been found in the

TABLE 5

Results from Other Forms

Category	Transformation	Exper. Mean	Control Mean	Mean Diff.	F	Open Mean	Closed Mean	Mean Diff.	F
Ride slips	cube root	3.02	3.30	.28	—	1.76	4.56	2.80	19.9 P>.001
Building cards	cube root	.54	.57	.03	—	.19	.93	.74	14.24 P<.01
Visitor slips	log of raw scores	19.19	18.09	1.10	—	8.72	28.56	19.84	148.6 P>.001
Transfers from A and B Building	cube root	.43	.67	.24	—	.19	.91	.72	23.98 P<.001
Transfers from other buildings or wards	cube root	.43	.30	.13	—	.19	.54	.35	9.33 P<.01
LOA releases	square root	7.17	8.15	.98	—	9.37	4.83	4.54	95.9 P<.001
LOA returns	raw score	6.67	7.67	1.00	—	9.83	4.50	5.33	105.33 P<.001

TABLE 6

Percentage of Time Spent in Various Activities by Ward Nurses

	WARDS							
	Closed Experimental			Open Experimental				
Area	Day Nurse	Day Nurse	P.M. Nurse	Day Nurse	Day Nurse	P.M. Nurse	Closed Control	Open Control
Physical treatment								.5
Indirect physical treatment	10	5	2.5	2.5	2.5		12.5	
Doctor directed psychotherapy	22.5	20	2.5	7.5	5		10	10
Nurse initiated psychotherapy	30	37.5	55	50	47.5	60	47.5	42.5
Ward reports	7.5	2.5	7.5		5	7.5		2.5
Personnel centered activities	5	2.5		5	5	2.5	7.5	7.5
Management activities								2.5
Clerical activities			2.5	5	2.5	5		
Housekeeping activities			2.5		7.5	5	2.5	2.5
Messenger activities	10	2.5	7.5	7.5	5	2.5	5	2.5
Personal time	15	30	20	22.5	17.5	17.5	15	20
Stand by time					2.5			

to days in residence. The results are shown measures utilized by this study.

Secondly, it was impossible to control the rapid turnover of patients. Since this study was conducted in an area which had to continue its service function it was not possible to "freeze" the patients on their ward for the duration of the study. When a patient's behavior became no longer suitable for the ward on which he had been residing it was necessary to transfer him to an area which could handle his degree of illness. Also, when a patient became well enough for discharge, he was released. As a result even though the study lasted six months, there were few patients who actually were exposed to the experience of increased nursing care for this period. If it could have been arranged that the population in the study would have been constant, it is possible that the results would have shown that additional nurses did bring about greater improvements.

The results do show, however, what happens to a ward when more nurses are put there. It clearly demonstrates that, if more things are to be done for patients and if more patients are to be introduced to more activities, it can be accomplished by additional nurses. The primary problem, which we have failed to solve, is an empirical demonstration that there is a corresponding movement out of the hospital when more nurses are utilized.

The study demonstrates yet another observation. When more nurses are added, their skills tend to be applied where they are needed most—with patients who are slower in responding to the regular hospital program. This is an important group to reach, because it is from this group that the additional remissions must come if there is to be an appreciable increase in a mental hospital's discharge rate.

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Christiana Burke, R.N., former Director of Nursing, Northville State Hospital, Christy Hawkins, R.N., Alice Parinello, R.N., and Aurelia Norton also made substantial contributions to this investigation.

REFERENCES

Burke, C., Chall, C. L., and Abdellah, F. G.: A Time Study of Activities in a Psychiatric Hospital. *Nursing Research,* 5:27-35, June 1956.

Deprol in Depressive Conditions

KARL RICKELS, M.D., and JAMES H. EWING, M.D.

Several new drugs have been introduced recently for the treatment of depressive conditions. Deprol, a combination of meprobamate and benactyzine, interested us because of the previously observed fact[2] that meprobamate alone already possesses certain antidepressive properties; particularly when administered in dosage higher than usually used in the treatment of anxiety conditions, and when given to patients who exhibit a certain amount of anxiety and tension, even if their psychomotor activity is slightly retarded. The addition of benactyzine is considered to be beneficial as it seems to relieve the ruminative obsessive aspects of the depressive mood.[1]

After an initial observation period, Deprol was given to 25 psychotic in-patients suffering from depression, irrespective of diagnosis, and to 10 neurotic out-patients diagnosed as mild reactive depressions with anxiety. Most of the in-patients exhibited additional symptoms of anxiety and tension and the balance were of a retarded and withdrawn type. Administration of placebo or meprobamate in identical capsules was used as control in a blind design by substituting them in half of the 25 in-patients, who showed at least some improvement with Deprol, and by using them in a randomized design with Deprol in the 10 neurotic depressions. All in-patients were seen at least twice weekly by a resident, the research physician and research nurse and data were pooled for improvement rating. The ten out-patients were seen biweekly and were kept on Deprol and placebo for periods of two weeks each. Most patients remained on Deprol after their return to their private physician.

All in-patients were subjected to a varying amount of psychotherapy while on Deprol, since our hospital focuses on treating acutely ill patients intensively for a relatively short period of time.

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Improvement was rated on a four point scale (4=no change or worse, 3=mild, 2=moderate and 1=marked improvement). Mild improvement was defined as any small change which was detected by any of the three observers. Moderate change meant that agreement existed among all observers that a definite change had occurred in the patient, at least facilitating psychotherapy. Marked improvement was defined as alleviation of all depressive symptoms.

The patients, equally divided as to sex ranged in age from 17 to 57 with an average age of 38 and fell into several diagnostic categories as seen in Table 1. Dosage ranged from 4 to 12 tablets daily with an average of 8 tablets. While 10 in-patients received Deprol for a period of only 5-20 days, the remaining in-patients received Deprol for over 20 days, up to 120 days (1 patient). Degree of improvement was not related to number of days on the drug, as long as the patient received Deprol for over 10 days. The 10 neurotic out-patients received Deprol for two weeks.

TABLE 1

Deprol in Patients Manifesting Depressive Symptomatology

Diagnosis	No. Pts.	Degree of Improvement: None	Mild	Moderate	Marked
Schizophrenic reaction, paranoid and catatonic type	9	3	3	2	1
Schizophrenic reaction, schizoaffective type	2			1	1
Pseudoneurotic schizophrenia	1		1		
Psychotic depressive reaction	11	1	3	4	3
Manic depressive reaction, depressed type	2	1		1	
Total psychotic reactions	25	5	7	8	5
Neurotic depressive reaction	10	1	2	5	2
Total number of patients	35	6	9	13	7

Drowsiness on higher dosage as well as two incidences of dizziness and one of syncope and vomiting were the only side reactions noted.

Results

Results are presented in Table 1. Two unimproved psychotic patients and one patient showing only mild change were placed on electroshock and all three improved markedly. Eight in-patients had been on a prior trial of iproniazid. One of them did not change and one improved mildly on both drugs while six patients improved to varying degrees only while on Deprol. Seven in-patients were later placed on meprobamate, four maintained improvement and three got worse; six in-patients were placed on placebo and all became worse. Of the 10 neurotic out-patients, seven felt better on Deprol than on placebo as reported subjectively by the patient and measured by our rating scale.

Conclusion

In our series of patients suffering from varying degrees of depression, Deprol, in conjunction with milieu and various forms of psychotherapy, did benefit a considerable number of patients. The improvement under Deprol consisted mainly in lessening of general depressive mood without euphoria, producing more interest in the surroundings (libido extension), lessening of fear, apprehension, panic and anxiety and marked reduction of irritability, crying spells and insomnia. Patients who manifested marked delusions and hallucinations were least influenced. In a great number of our patients Deprol definitely facilitated psychotherapy while it was much less effective without it.

Authors' Note: Deprol is the trademark of Wallace Laboratories for the combination of 400 mg. of meprobamate and 1 mg. of benactyzine. Deprol and placebo were provided by Wallace Laboratories, New Brunswick, N. J.

BIBLIOGRAPHY

1. Alexander, L.: *J.A.M.A.*, 166:1019, March 1, 1958.
2. Ruchwarger, A.: *Med. Ann. Dist. Columbia*, 25: 555, October, 1956.

The History and Pharmacology of the Ataractic Drugs

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General

Agents previously available for sedative purposes consisted primarily of the barbiturates, paraldehyde, narcotics, chloral hydrate, bromides, and other allied drugs. With larger doses of these drugs, it was often found that the patient was subjected to depression of the vital centers, and the sedatives were disabling in effective doses. In addition to this, this drug dependency would likely perpetuate underlying psychiatric disturbances and dependency needs. The term atarax comes from the Greek, *ataraxia*, meaning without discomfort. A large group of drugs come largely under this category and consist primarily of the phenothiazines, rauwolfia derivatives, diphenyl methanes and propanediols.[18]

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Presented to Lake County Medical Society April 8, 1958.

Physiological Considerations

The physiological effects[15] of these drugs in therapeutic doses are generally due to an inhibition of the subcortical centers primarily in the region of the hypothalamus. Chlorpromazine, one of the phenothiazine drugs, depresses the brain stem reticular formation, (BSRF) which with its thalamic diffuse projection system (TDPS), form the mesodiencephalic activating system (MD AS). In larger therapeutic doses, however, this particular drug stimulates the MDAS. It has been shown experimentally[6] that stimulation of the reticular pathways particularly in the region of the midbrain tends to be associated with anxiety, therefore, the paradoxical effect of sedation evidently is likely due to the more pervasive inhibiting effect of the autonomic centers in the region of the hypothalamus. Reserpine, a representative of the rauwolfia group, stimulates the BSRF

and the higher projection pathways and its sedative effect is believed to be directly due to the inhibition of the hypothalamic centers. Meprobamate (Miltown or Equanil) is a member of the propanediol group. This drug inhibits the internuncial circuits between the cerebral cortex and the thalamus. Frenquel (azacyclonol), a member of the diphenyl methane group, seems to have a sedative effect and is particularly effective in counteracting toxic psychosis of LSD-25.[3] Its effect seems to be that of inhibition of the subcortical centers.

Propanediols

The propanediols[19] were discussed by Berger in 1954 with a special reference to mephenesin, a prototype of meprobamate, in its use to relieve muscular tension. Di-isopropylfluorophosphate (DFP) worked, but was short acting. Meprobamate, which was developed from the above studies, was noted to have longer action with less side effects, and in addition, found to have a sedative action. The mode of action in this drug seems to be primarily that of an inhibitory effect on the CNS with anticonvulsive properties. There is no direct effect on the muscle, neuromuscular junction or in the peripheral nerves, but there seems to be blocking of the interneurons in the thalamus and caudate nucleus. There seems to be virtually no effect on the autonomic nervous system (ANS), G.I. tract, pressor responses or respiratory system. The toxicity seems to be low, about one fifth of most barbiturates, and the side effects consist of transient headaches, G.I. discomfort, occasional allergy and fainting, and few other disturbances of significance. Additional properties have been noted recently.

Diphenyl Methane Compounds

The diphenyl methane compounds consist of azacyclonol (Frenquel), benactyzine (Suavitil) and hydroxyzine (Atarax). These drugs were further developed from studies on meratran,[5] Frenquel, which is a G isomer of meratran, has a stimulant effect on the MDAS without other apparent significant effects on the ANS. This drug has been shown to be antagonistic to the hallucinogenic drugs like LSD-25. It would seem that LSD stimulates the production of serotonin in low doses and Frenquel inhibits serotonin. Serotonin is regarded by some investigators to produce hallucinogenic-like states. It has been shown experimentally[3] that serotonin has properties somewhat similar to LSD-25 and its precursor, 5-hydroxytrypophan (5-HTP), produced marked effects in doves which were similar to those produced by LSD. It has been noted[3] that there is a hyperserotinemia produced in the carcinoid syndrome with the production of vasomotor disturbances, bronchoconstriction, intestinal hypermotility and valvular heart disease. The relationships of these chemicals and adrenalin with its oxidation product adrenochrome[8] are the subject of much further experimentation to determine if there is any relationship between inborn or acquired errors of metabolism and the syndrome of schizophrenia.[1,3,7,13,14,16,17] It should be noted that the syndrome of phenylketonuria, which is one of the inborn errors of metabolism,[13] is usually accompanied by a mental deficiency. It would appear that phenylalanin is not broken down to tyrosine in this disorder. These bio-chemical factors are intimately connected biologically with adrenalin and noradrenalin.

Iproniazid

Another stimulant drug which is being used is known as iproniazid (Marsilid) which has been involved with the treatment of tuberculosis was studied by Selikoff and others in 1952. During that time they also noted that there was an improvement in appetite and from apathy. The mode of action of this drug, which is a psychic stimulant, is believed to be due to the accumulation of serotonin to a fairly high level, due to the inhibition of monoamine oxidase. Reserpine, which is a psychic depressant, releases serotonin on a low level from its bound forms of storage in the brain, platelets and bowel. A combination of iproniazid and Reserpine gives an LSD-like effect. Side effects, due to increased sensitivity to stimulation, consist of dizziness, tinnitus, paresthesias, increased muscle tonus, ANS imbalance including dry mouth, constipation, dysuria, diaphoresis, flushing and hypotension. At time

there is euphoria, insomnia, increased psychomotor activity, and occasionally psychosis, especially on higher dosages.

Meratran

Meratran (Pipradol) has been developed by Merrell and is a piperidine derivative. The mode of action of this drug seems to produce purposeful hyperactivity by stimulation of the BSRF without convulsions. The side effects are said to be mild and infrequent, consisting of drowsiness, dizziness, skin reactions, and at times mild extrapyramidal symptoms.

Ritalin

Ritalin, a piperidine derivative, was developed by CIBA[2] in 1956. This drug is a stimulant of the central nervous system inducing mental alertness. It is not a sympathomimetic amine. It is an antagonist to CNS depressants such as barbiturates and chloral hydrate. The side effects are said to be minimal and consist of tension, insomnia, anorexia, nausea, dizziness, palpitation and headaches.

The Rauwolfia Drugs

Historically[2] these drugs have been used for several centuries. The roots of the serpentina plant were used in crude extracts as far back as 1573 by a Leonhard Rauwolf, who was a physician and in accordance with the custom at that time went around the world picking up drugs and roots for pharmacological purposes. It was noted that the crude extracts of these roots had sedative properties but it was not until the twentieth century that this became publicized in the Indian medical literature. In 1931, Siddiqui of India discussed five different alkaloids from this plant. In 1933, Bhatia used some of these extracts in hypertension. In 1947 Schlittler and his colleagues in Switzerland isolated ajmaline for the Ciba Corporation. After considerable effort, 100 grams of this particular drug was sent to Sir Robert Robinson of England in 1948 for clinical use. In 1951 and 1952 Reserpine was developed by the Ciba Laboratories and since that time has been used in increasing amounts for various conditions, including hypertension and psychiatric disorders. The latter usage of this drug has increased considerably since 1954. The physiological considerations of Reserpine indicate that its mode of action seems to be chiefly on the pressor regulatory centers in the region of the hypothalamus due to inhibitory mechanism. It is not a ganglionic block nor an adrenolytic agent In small doses, it stimulates the BSRF, has very little anticonvulsive action and is an antagonist to the antiepileptic drugs. It interferes with the metabolism of serotonin which is also theoretically[3,10] involved in the production of psychotic disorders. Clinically there is a gradual lowering of blood pressure with little effect in rate, a partial supression of the sympathetic centers in the region of the hypothalamus and facilitation of the cortical acting stimulant such as caffeine and metrazol. It has autonomic nervous system effects by symptoms of bradycardia, hypotension, miosis, ptosis and hyperperistalsis. The side effects of both these drugs generally consist of parkinsonism, especially in the larger doses, a tendency to liver damage with a production of jaundice which is seldom serious, mild G.I. disturbances, weakness, lethargy and a marked tendency to drowsiness, skin manifestations, at times blood disturbances including agranulocytosis (at times lowering of all blood element formation), convulsions and even psychotic manifestations.

Phenothiazines

The historical aspects[11] of these drugs are quite interesting. The phenothiazine compounds have been derived from tests performed at the Rhone Poulenc Laboratories near Paris, France, where experiments were being done in using derivatives of this compound in trypanosomiasis and malaria. In December of 1950, Charpentier synthesized 4560 RP which was later known as Largactil in 1952. In that same year Laborit, et al., synthesized Phenargan (promethazine) which was used in artificial surgery. Chlorpromazine was developed in 1952 by Harmon, Paraire, Delay, Deniker, Harl and others.[4] This was used in anesthesia when it was noted that a sedative and hypotensive effect were produced. The drug began to be used for these effects later. In the early part of 1954 this drug was used in Canada by

Lehmann and Hanrahan[11] in the treatment of psychiatric disorder and was finally introduced into the USA in the early part of 1954 by Winkleman. To illustrate the extent to which ataractic drugs are used, the gross sales for one drug amounted to about 15 million dollars in one year. Thorazine has been used widely in private practice for adjuncts to anesthesia, sedation, nausea and vomiting, hiccoughs, pain, hypertension and emotional and psychiatric disorders of varying degrees. Some of the derivatives of phenothiazine used in practice today, consist of chlorpromazine (Thorazine); diethazine (Diparcol); ethopromazine (Parsidol); mepazine (Pacatal); Phenothiazine (XL 50); prochlorphenazine (Compazine); promazine (Sparine); pyrrolazate (Parathiazine); trifluprom azine (Vesprin) and thiopropazate (Dartal).

The physiology and pharmacological characteristics of chlorpromazine indicate that it is a quick-acting, strong central sedative. It has adrenergic and cholinergic blocking action. Its antiemetic action is said to be due to inhibition of the vagal eminence in the fourth ventricle. It also has hypothermic and antihistaminic activity. It has a sparing action on adenosine triphosphate (ATP) catabolism especially in hypothalamic area. The drug also acts on the central nervous system especially on parts of the brain stem in the region of the subthalamic nucleus, red nucleus, substantia nigra, and the BSRF area in the region of the hypothalamus.

Discussion

The ataractic drugs seem to produce their sedative effect by depression of the hypothalamic centers, especially the sympathoadrenal system. The MDAS have both adrenergic and cholinergic functions and likely are the pathways for correlative function with the higher cerebral centers. The neurophysiological action apparently involves the enzyme (oxidase) factors including the metabolism of phenylalanine, adrenal-medullary amines, carbohydrates, in which serotonin, adrenochrome, mono-amine oxidase, the Krebs cycle ceruloplasmin, and noradrenalin seen to play important parts. The production of toxic psychosis by the hallucinogenic drugs leads to speculation as to the enzymatic role in the probable pathological physiology in the brain of the schizophrenic. Inborn errors of metabolism seem to be a possibility. Some of the drugs (energizers) have stimulative function and are used to help alert the depressed and retarded patient. Side effects and complications are not uncommon and diligent care is necessary in use of these drugs especially in the larger doses.

Summary

1. The historical, neurophysiological and pharmacological aspects of the ataractic drugs have been briefly discussed.

2. Theoretical relationships between errors in the enzyme systems as possible factors in the pathological physiology of disordered mental functions is being investigated on a comprehensive scale.

3. The mode of action of the ataractic drugs seems to be largely in the vicinity of the hypothalamus.

BIBLIOGRAPHY

1. Brodie, B. B., Olin, J. S., Kuntzman, R. G., and Shore, P. A.: Possible Interrelationship Between Release of Brain Norepinephrin and Serotonin by Reserpine. *Sci.*, 125: 1293-1294, June 1957.
2. Ciba: Serpasil in Psychiatry. 1st Ed. Summit, N. J., Aug. 1955.
3. Davidson, J., Sjoerdsma, A., Loomis, L. N., and Underfriend, S.: Studies with the Serotonin Precursor, 5-hydroxytroptophan in Experimental Animals. *J. Clin. Invest.*, 36: 1594-1599, Nov. 1957.
4. Delay, J., Deniker, P., and Tardieu, Y.: Hibernation Therapy and Therapeutic Narcosis in Psychiatric and Psychosomatic Therapy. *Press Med.*, 61: 1165-1166, Sept. 1953.
5. Fabing, H. D.: Frenquel, a Blocking Agent Against Experimental LSD-25 and Mescaline Psychosis. *Neurology*, 5: 319-328, May 1955.
6. Gellhorn, E.: Physiological Processes Related to Consciousness and Perception. *Brain*, 77: 401-415, 1954.
7. Heath, R. G., Leach, B. E., Byers, L. W., Martens, S., and Feigley, C. A.: Pharmacological and Biological Psychotherapy. *Am. J. Psychiat.*, 114: 683-689, Feb. 1958.
8. Lea, A. J.: Adrenochrome as the Cause of Schizophrenia. *J. Ment. Sci.*, 538-547, July 1955.
9. Lehmann, H. E., and Hanrahan, G. E.: Chlorpromazine. *Arch. of Neurol. and Psychiat.*, 71: 227-237, Feb. 1954.
10. Marazzi, A. S.: The Possible Role of Inhibition at Adrenergic Synapses in the Mechanism of Hallucinogenic and Related Drug Action. *Nerv. and Ment. Dis.*, 122: 453-457, Nov. 195...

11. Marti-Ibanez, F., Sackler, A. M., Sackler, M. D., and Sackler, R. R.: Chlorpromazine. *J. Clin. and Exper. Psychopathol.*, 17: 15-18, Mar. 1956.

12. Papez, J. W.: Central Reticular Path. to Intralaminar and Reticular Nuclei of Thalamus for Activating EEG Related to Consciousness. *J. EEG & Clin. Neurophysiol.*, 8: 117-128, Feb. 1956.

13. Penrose, L. D.: Inborn Errors of Metabolism in Relation to Mental Pathology, pps. 807-817 in Neurochemistry by Elliot, K. A. C., Page, I. H., and Quastel, J. H., Springfield, Ill., *Charles C. Thomas*, 1955.

14. Porter, C. C., Titus, D. C., Sanders, B. E., and Smith, C. V. C.: Oxidation of Serotonin in the Presence of Ceruloplasmin. *Sci.*, 126: 1014-1015, Nov. 1957.

15. Rinaldi, F., and Himwich, H. E.: Drugs Affecting Psychotic Behavior and the Function of the Mesodiencephalic Activating System. *Dis. Nerv. Syst.*, 16: 133-141, May 1955.

16. Savage, C., and Cholden, L.: Schizophrenia and the Model Psychoses. *J. Clin. and Exper. Psychopathol.*, 17: 405-13, Dec. 1956.

17. Thompson, R. H. S., Tickner, A., and Webster, G. R.: The Action of Lysergic Acid Diethylamide on Mammalian Cholinesterases. *Brit. J. Pharm.*, 10: 61-65, Mar. 1955.

18. Truitt, E. B.: Pharmacology of the Ataractic Drugs. *Mod. Med.* 25: 77-81, Jan. 1957.

19. Wyeth: Equanil, Philadelphia, Pa., 1956.

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